COPYRIGHT DEPOSIT

INDEX NUMBER

Vol. 16 DECEMBER, 1944 No. 6

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

EDITORS

ALTON OCHSNER, New Orleans OWEN H. WANGENSTEEN, Minneapolis

ASSOCIATE EDITOR

ALFRED BLALOCK, Baltimore

JAN 31 1945

CONTENTS

Original Communications

Esophageal Duplications or Mediastinal Cysts of Enteric Origin. William E. Ladd, M.D., and H. William Scott, Jr., M.D., Boston, Mass. ---- 815
Primary Lymphosarcoma of the Breast. Frank E. Adair, M.D., and Julian B. Herrmann, M.D., New York, N. Y. ---- 836
Mixed Malignancy of the Breast. H. G. Smithy, M.D., Charleston, S. C. ---- 854
Boeck's Sarcoid. Major Ira Gore, and Lieutenant Colonel Alphonsus M. McCarthy, M.C., A.U.S. ---- 865
Compound Craniocerebral Injuries. William J. German, M.D., Bernard S. Brody, M.D., and Samuel C. Harvey, M.D., New Haven, Conn. ---- 874
Improved Retractor for Hemilaminectomy. Lieutenant C. Hunter Shelden, and Lieutenant Robert H. Pudenz, Medical Corps, U.S.N.R. ---- 884
A Limited Comparison of Continuous Spinal and General Ether Anesthesia. William Grant Cooper, II, M.D., Wilma Zumwalt, R.N., and Everett D. Sugarbaker, M.D., Columbia, Mo. ---- 886
Cystometry After Spinal Anesthesia. Major Carroll J. Bellis, M.C.Res., U.S.A. 896
A Demonstration of Two Types of Burn Shock. Myron Prinzmetal, M.D., H. C. Bergman, Ph.D., and Oscar Hechter, Ph.D., Los Angeles, Calif. ---- 906
Further Studies on the Role of Bacteria in Shock Due to Crushed Muscle in Dogs. S. C. Freed, M.D., H. E. Kruger, and Myron Prinzmetal, M.D., San Francisco, Calif. ---- 914
The Retention of Intravenously Infused Gelatin. Alexander Brunschwig, M.D., and Sabra Nichols, B.S., Chicago, Ill. ---- 923
Intestinal Obstruction. I. The Protective Action of Succinylsulfathiazole Following Simple Venous Occlusion. Stanley J. Sarnoff, M.D., and Edgar J. Poth, M.D., Ph.D., Galveston, Texas ---- 927
The Application of Succinylsulfathiazole and Phthalysulfathiazole to Granulation Tissue: Absorption and Excretion. Edgar J. Poth, M.D., Ph.D., and Charles A. Ross, M.S., Galveston, Texas ---- 932
A Method for the Local Administration of Penicillin. Colonel Elliott C. Cutler and Major William R. Sandusky, Medical Corps, U. S. Army ---- 937
Primary Carcinoma of Third Portion of Duodenum. Thomas A. Shallow, M.D., Sherman A. Eger, M.D., and James B. Carty, M.D., Philadelphia, Pa. 939
Spontaneous Ventral Hernia. Edward Woliver, M.D., and Charles M. Scott, M.D., Cincinnati, Ohio ---- 947
Congenital Eventration at the Umbilicus. Alfred H. Iason, M.D., Brooklyn, N. Y. 950
A Sharp Dissector for Meniscectomy. Captain Raymond E. Buirge, M.C., U.S.A. 956

Notices

Notices ---- 959
Books Received ---- 961
Index ---- 963

Published by THE C. V. MOSBY COMPANY, St. Louis, U. S. A.

Copyright 1944 by The C. V. Mosby Company

JAN 29 1945

SURGERY

ADVISORY COUNCIL

DONALD C. BALFOUR, Rochester, Minn.
VILRAY P. BLAIR, St. Louis
BARNEY BROOKS, Nashville
ELLIOTT C. CUTLER, Boston
WILLIAM E. GALLIE, Toronto
EVARTS A. GRAHAM, St. Louis
HOWARD C. NAFFZIGER, San Francisco
HARVEY B. STONE, Baltimore
ALLEN O. WHIPPLE, New York City

EDITORIAL BOARD

FREDERICK A. COLLER, Ann Arbor
EDWARD D. CHURCHILL, Boston
VERNON C. DAVID, Chicago
LESTER R. DRAGSTEDT, Chicago
RALPH K. GHORMLEY, Rochester, Minn.
ROSCOE R. GRAHAM, Toronto
SAMUEL C. HARVEY, New Haven
FRANK HINMAN, San Francisco
EMILE F. HOLMAN, San Francisco
EDWIN P. LEHMAN, University, Va.
FRANK L. MELENEY, New York City
JOHN J. MORTON, Rochester, N. Y.
THOMAS G. ORR, Kansas City, Kan.
GEORGE T. PACK, New York City
WILDER G. PENFIELD, Montreal
ISIDOR S. RAVDIN, Philadelphia
WILLIAM F. RIENHOFF, JR., Baltimore

COMMITTEE ON PUBLICATIONS

ARTHUR W. ALLEN
Boston, Mass.

CLAUDE S. BECK
Cleveland, Ohio.

ELEXIOUS T. BELL
Minneapolis, Minn.

ISAAC A. BIGGER
Richmond, Va.

ALBERT C. BRODERS
Rochester, Minn.

J. BARRETT BROWN
St. Louis, Mo.

ALEXANDER BRUNSCHWIG
Chicago, Ill.

LOUIS A. BUIE
Rochester, Minn.

WARREN H. COLE
Chicago, Ill.

C. D. CREEVY
Minneapolis, Minn.

GEORGE M. CURTIS
Columbus, Ohio

M. DE BAKEY
New Orleans, La.

JOHN STAIGE DAVIS
Baltimore, Md.

WILLIAM J. DIECKMANN
Chicago, Ill.

DANIEL C. ELKIN
Atlanta, Ga.

WILLIS D. GATCH
Indianapolis, Ind.

CHARLES F. GESCHICKTER
Baltimore, Md.

J. SHELTON HORSLEY
Richmond, Va.

J. MASON HUNDLEY, JR.
Baltimore, Md.

ANDREW C. IVY
Chicago, Ill.

DENNIS E. JACKSON
Cincinnati, Ohio

J. ALBERT KEY
St. Louis, Mo.

CHAUNCEY LEAKE
San Francisco, Calif.

FRANCIS E. LEJEUNE
New Orleans, La.

HAROLD I. LILLIE
Rochester, Minn.

JOHN S. LUNDY
Rochester, Minn.

FRANK C. MANN
Rochester, Minn.

CHARLES W. MAYO
Rochester, Minn.

ROBERT L. PAYNE
Norfolk, Va.

LEO G. RIGLER
Minneapolis, Minn.

ERNEST SACHS
St. Louis, Mo.

ARTHUR M. SHIPLEY
Baltimore, Md.

ALBERT O. SINGLETON
Galveston, Texas

MAURICE B. VISSCHER
Minneapolis, Minn.

RALPH M. WATERS
Madison, Wis.

JAMES C. WHITE
Boston, Mass.

PHILIP D. WILSON
New York, N. Y.

JOHN A. WOLFER
Chicago, Ill.

Vol. 16, No. 6, December, 1944. Surgery is published monthly by The C. V. Mosby Company, 3525 Pine Blvd., St. Louis 3, Mo. Subscription price: United States, its possessions, Pan-American Countries, $10.00 a year; Canada, $11.50 (Canadian Currency); Foreign, $11.00. Entered as Second-Class Matter January 20, 1937, at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Printed in U. S. A.

COPYRIGHT DEPOSIT

Consistently proving their

SUPERIORITY...

RIB-BACK BLADES

feature undeviating qualities that facilitate the more successful attainment of the surgical objective

IN COMBINATION, the distinctive features which characterize these widely preferred surgical blades afford the optimum in cutting efficiency. They provide superior sharpness with uniformity. Greater strength is attained by the exclusive application of the Rib principle of blade reinforcement. All are qualities which contribute to long periods of satisfactory service and virtually eliminate the element of distractive influence.

The quality of Rib-Back Blades has suffered no wartime change. They continue to be offered at the lowest price consistent with their inimitable precision qualities.

Ask your dealer

BARD-PARKER COMPANY, INC.

Danbury, Connecticut

A BARD-PARKER PRODUCT

Therapy in Nutritive Failure

IN MANY, if not most disease states, the therapy of nutritive failure is important in hastening convalescence and restoring the patient to a state of health.

The four essentials for therapy in nutritive failure include . . .

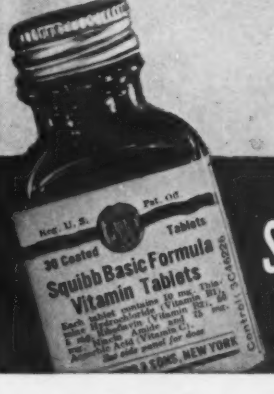
1. **DIET:** 4,000 calories, 150 gram protein, rich in vitamins and minerals.
2. **BASIC THERAPY:** Thiamine, riboflavin, niacinamide, ascorbic acid, orally.
3. **ADDITIONAL MEDICATION:** Synthetic vitamins as indicated orally or parenterally.
4. **NATURAL B COMPLEX:** Brewers' Yeast or extract, or rice bran extract, and/or liver extract orally or parenterally.

The Squibb Laboratories provide three of the four essentials for such therapy. They provide BASIC FORMULA VITAMIN TABLETS for intensive BASIC THERAPY—note their content:

10 mg. Thiamine Hydrochloride
50 mg. Niacinamide
5 mg. Riboflavin
75 mg. Ascorbic Acid

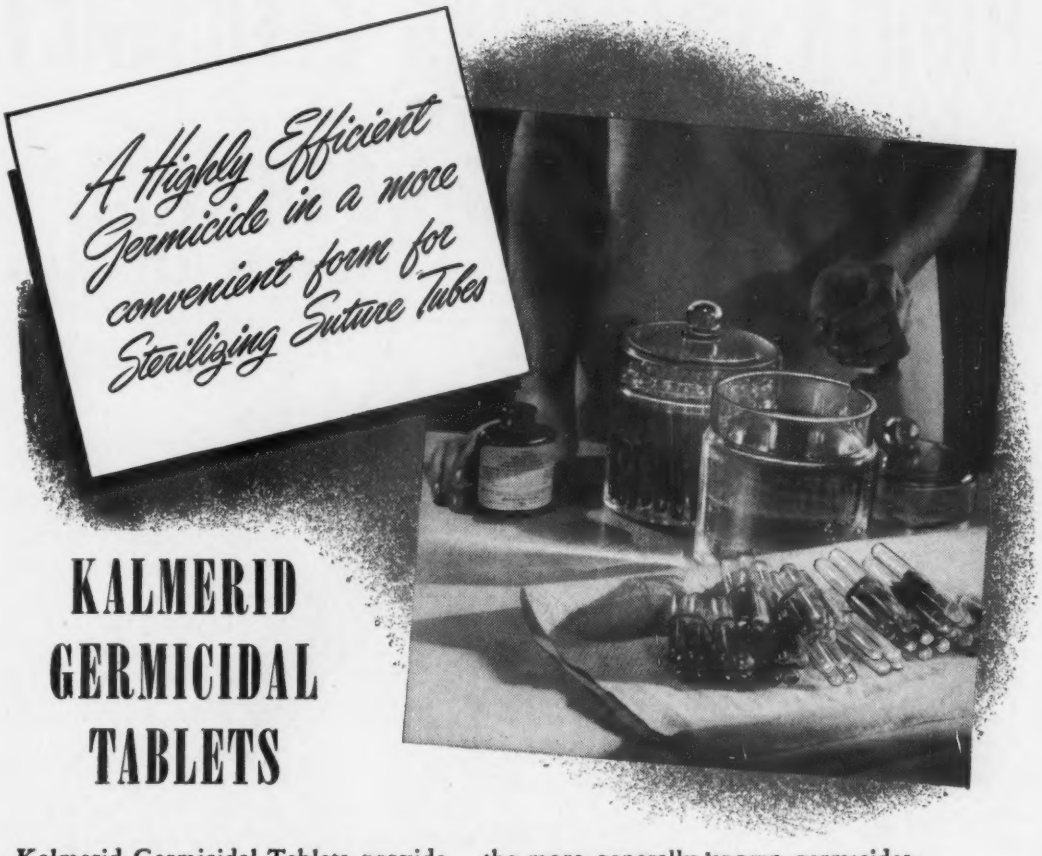
This is the basic formula used by Drs. N. Jolliffe and T. D. Spies and described by the latter in his paper on Nutritional Rehabilitation of 100 American workers for Industry.

Squibb also proyides the synthetic vitamins indicated for *additional medication* as well as the *natural B Complex* factors—the fourth essential therapy of nutritive failure.



Sold to druggists in bulk. . . . Prescribe as few or as many tablets as may be needed. . . . The cost per tablet is surprisingly low. . . . Write for literature.

Squibb Basic Formula Vitamin Tablets



KALMERID GERMICIDAL TABLETS

Kalmerid Germicidal Tablets provide potassium-mercuric-iodide—a valuable antisepticizing and disinfecting agent —in a *pure, stable,* soluble and convenient form for the sterilization of suture tubes. A solution of one Kalmerid Germicidal Tablet in one liter of 70% alcohol makes a reliable and easily prepared medium. In this solution the tubes sink of their own weight and remain completely submerged.

Potassium-mercuric-iodide has advantages over certain of the more generally known germicides for a variety of other uses also. It exceeds bichloride of mercury in bactericidal potency, is readily soluble, comparatively low in toxicity, free from irritant action, and forms no soluble combinations with proteins.

Solutions of any strength may be made easily and efficiently with Kalmerid Germicidal Tablets.

Further information on their action, uses and advantages will be sent promptly on request.

DAVIS & GECK, INC.

57 WILLOUGHBY STREET, BROOKLYN 1, N. Y.

D&G SUTURES ARE OBTAINABLE THROUGH RESPONSIBLE DEALERS EVERYWHERE

HIGHER OPERATING EFFICIENCY

WITH THE

SINGER SURGICAL STITCHING INSTRUMENT

Many ingeniously designed instruments have contributed, particularly in the last decade, to the extraordinarily high operating efficiency of the modern surgeon.

Yet it has remained for the Singer Surgical Stitching Instrument to place real suturing capacity in the operator's own hand.

This precision-made instrument eliminates the elaborate sterilizing, threading and clamping preparation of numerous needles, and frees the operator from "hand-to-hand" dependence on surgical assistants. Stitching proceeds smoothly, deftly, rapidly — the instrument never leaving the surgeon's hand, even for knot tying. Indeed, the cutting of the suture material, too, may be dextrously completed with the keen knife-like edge of the lance-point needle.

The Singer Surgical Stitching Instrument is a surgical instrument of the highest quality — carefully balanced for easy manipulation in both deep and superficial fields. It employs any standard suture material, and may be fitted from a variety of available needle sizes, shapes and styles.

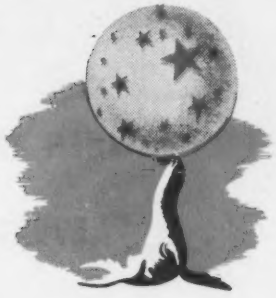
The instrument may be sterilized as a complete unit, or readily taken apart for cleaning and reassembly. All parts are rust-resistant.

Illustrated booklet furnished on request. Motion pictures demonstrating operative technique also available for group meetings. Write Dept. H-12

SINGER SEWING MACHINE COMPANY, *Surgical Stitching Instrument Division,* 149 BROADWAY, NEW YORK 6, N. Y.

Personal demonstration available at your local Singer Shop

Copyright U. S. A., 1944, by The Singer Manufacturing Co. All Rights Reserved for All Countries.



In Perfect Balance

When protein intake is inadequate or cannot be assimilated, Parenamine (Amino Acids Stearns) aids in restoring nitrogen balance.

This parenteral substitute for protein alimentation is often remarkably effective in accelerating the healing of burns and wounds—in shortening the convalescent period following surgery—when dietary conditions limit the intake of essential proteins.

Parenamine
Amino Acids Stearns

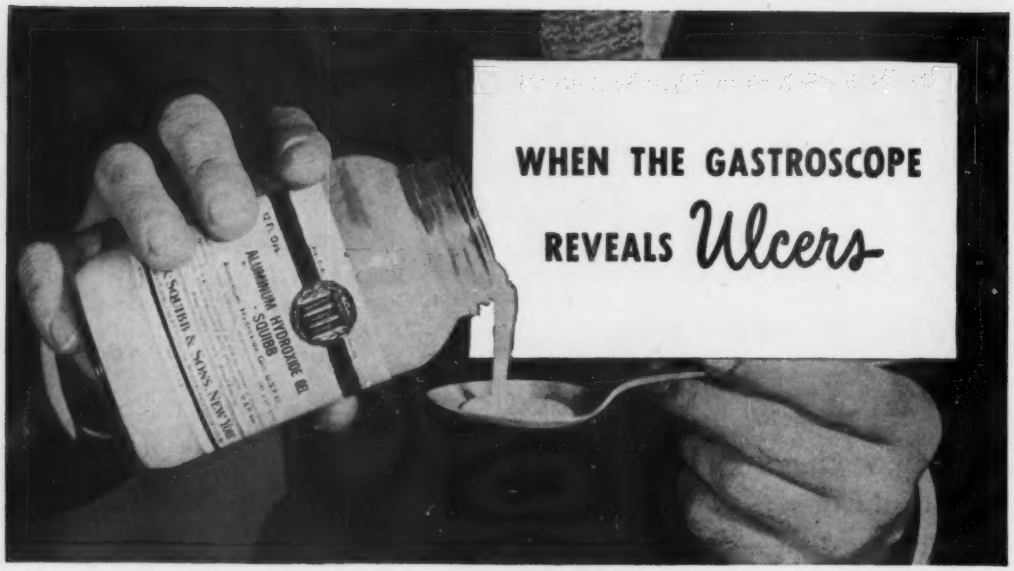
Available for parenteral and oral administration as a 15% solution in 100 cc. rubber-capped vials. Details of therapy available on request.
Trade Mark Parenamine *Reg. U. S. Pat. Office*

Frederick Stearns & Company

Division

DETROIT 31, MICHIGAN

NEW YORK · KANSAS CITY · SAN FRANCISCO · WINDSOR, ONTARIO · SYDNEY, AUSTRALIA · AUCKLAND, NEW ZEALAND



MODERN THERAPY includes the use of a non-absorbable alkali. For this purpose Aluminum Hydroxide Gel represents a marked advance in ulcer therapy, because it is capable of neutralizing large amounts of acid without inducing alkalosis.

Aluminum Hydroxide Gel Squibb offers several definite advantages. While complying with all U. S. P. XII specifications, it is sufficiently fluid not only to facilitate easy pouring, but also to make it particularly adaptable to dilution for use by the continuous intragastric drip method.

Aluminum Hydroxide Gel Squibb is a good-tasting aqueous suspension supplying approximately 1.85 grams aluminum hydroxide per fluid ounce. It may be used in milk soda mixtures if desired. Used alone, its pleasant flavor helps to combat the taste tedium of prolonged ulcer therapy.

For your convenience in prescribing, Aluminum Hydroxide Gel Squibb bears a descriptive name.

Supplied in 12-ounce bottles.

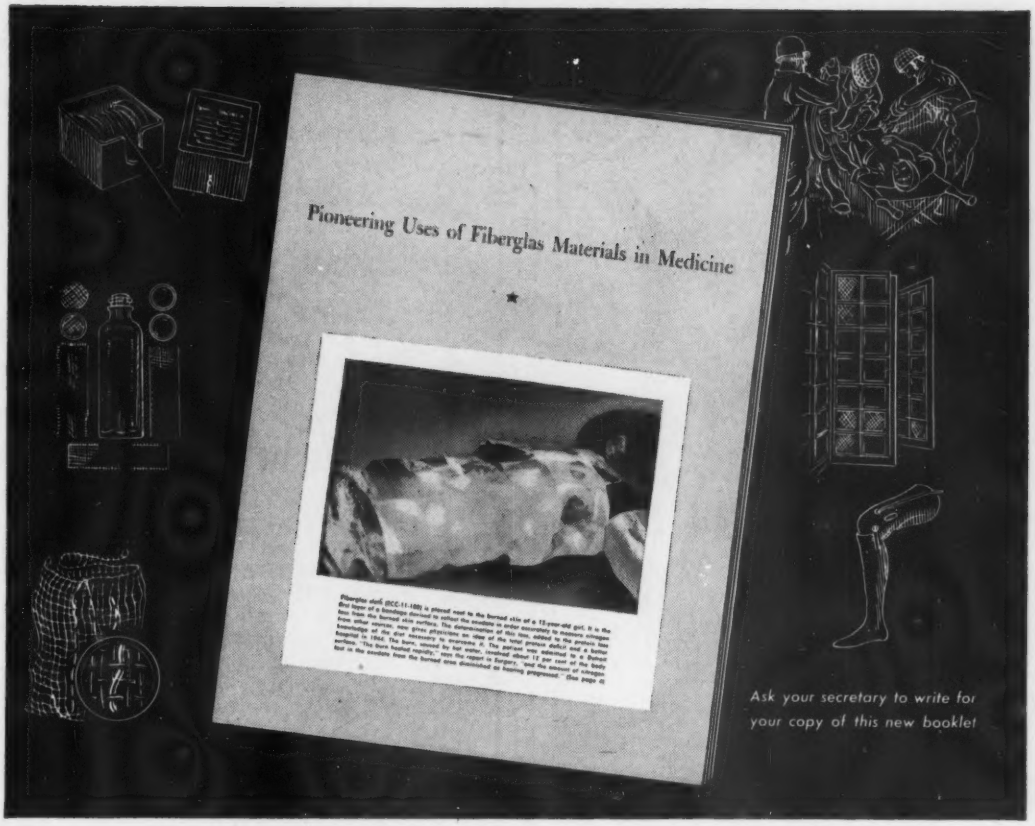
For literature address the Professional Service Dept., 745 Fifth Avenue, New York 22, N. Y.

E·R·SQUIBB & SONS

Manufacturing Chemists to the Medical Profession Since 1858

★ ★ ★

Buy Another War Bond . . . Now!



Pioneering Uses of Fiberglas Materials in Medicine*

This new booklet describes a few of the uses of Fiberglas in medicine. Some of the uses are still in the experimental stage and require further development. Others are now helping physicians and surgeons obtain improved results in treating the sick or wounded. Such uses include:

Measurement of Nitrogen Loss in Exudate from Burned Skin
Tracer Threads in Surgical Sponges
Experimental Surgical Sutures
Culture of Microorganisms
Blood Plasma Filters
Air-Borne Bacteria Control
Pollen and Dust Control
Penicillin Production
Insulation of Autoclavable Closed Motor
Fiberglas-Plastic Artificial Limbs

Fiberglas is glass in fiber or filament form. It is twisted into yarn, then woven into many types of textiles. A number of physical properties not often found in combination are responsible for the contribution Fiberglas has been able to make in the fields of research bearing on health.

Fiberglas is an inorganic, nontoxic, nonallergenic, nonsensitizing and chemically stable substance which produces no harmful effect upon human tissue. It is pliable, has great tensile strength, high dimensional stability and resistance to high temperatures, steam, corrosive fumes and acids (except hydrofluoric) and can be sterilized and resterilized. The individual fibers are nonhygroscopic and noninflammable.

Owens-Corning Fiberglas Corporation will produce and supply Fiberglas materials required for medical research and necessary to clinical investigation, regardless of the small quantities that may be involved.

In writing for your copy of the new booklet and Fiberglas sample card address: *Owens-Corning Fiberglas Corporation, 2034 Nicholas Bldg., Toledo 1, Ohio.*

FIBERGLAS

*T. M. Reg. U. S. Pat. Off.

ADVANTAGES of IODINE

The Iodine - wiped - off - with-alcohol technique in the preparation of the operative field kills bacteria rapidly and leaves the field dry, the skin clean.

Comparative tests demonstrate that Iodine is less affected by the presence of serum than many other similarly employed antiseptics.

IODINE
Foe of Infection

Iodine Educational Bureau, Inc.
120 Broadway, New York 5, N. Y.

Watson's
HERNIA
Featuring the Injection Treatment

by **LEIGH F. WATSON, M.D.**, Member of Attending Staff of California Lutheran Hospital and Methodist Hospital at Southern California, Los Angeles. 2nd Ed. 591 pages, 281 illustrations. Price, $7.50.

Hernia is an important surgical problem. There is more to it than a single method of treatment. To know about this condition you must be informed on all factors entering into its cause, what hernia involves, and the various methods for successfully treating each individual case. This information is given in the Second Edition of Watson's "Hernia." The coverage is complete—from Embryology to Legal Complications.

Every method of treatment—surgical and otherwise—is given, with special emphasis on Injection Treatment. Starting with an interesting historical introduction, the author considers the various types of hernias, local anesthesia in hernia operations, and the numerous operative procedures that experience has proved to be the best.

Illustrations are used profusely, making it easier to follow the suggested procedures. The anatomical details have been combined with the operative technique in the same drawings, thus greatly increasing the value of the illustrations. In all there are 281 illustrations.

Watson's "Hernia" is a well thought out and timely text, based on years of experience. Thanks to a great amount of clinical work and close observation this second edition offers you valuable help for the successful handling of your hernia problems.

The C. V. Mosby Company
Medical Publishers
St. Louis 3, Mo.

Reinforcing
the Effectiveness of Topical Sulfonamide Therapy

Sulfa-Ceepryn Cream, the improved sulfonamide cream reinforced with a germicidal detergent, is an important contribution to the therapy of pyogenic infections and burns, wounds and other lesions where infection is threatened.

SULFA-CEEPRYN

Brand

Sulfathiazole, Sulfanilamide and Cetylpyridinium Chloride

CREAM

COMBINATION OF SULFONAMIDES—Sulfathiazole 10% and sulfanilamide 10% provide *rapid* and *prolonged* bacteriostatic action of wider scope.

REINFORCED WITH CEEPRYN—Cetylpyridinium chloride 1:500 reinforces the sulfonamides with its powerful germicidal action, and its marked detergency aids penetration.

WATER-SOLUBLE BASE—A special vanishing cream base spreads evenly and releases medication readily.

One-ounce tubes and one-pound jars

Trademarks "Ceepryn" and "Sulfa-Ceepryn" Reg. U. S. Pat. Off.

MERRELL
116th Year

The Wm. S. Merrell Company • Cincinnati, U. S. A.

Completely conceals all skin discolorations—

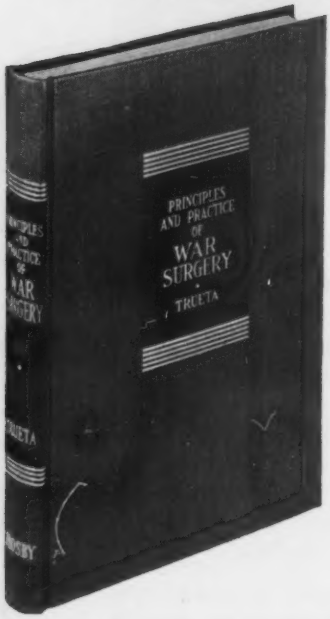
COVERMARK

for post-operative scars, birthmarks, vitiligo, etc.

LYDIA O'LEARY, INC., 551 FIFTH AVENUE, NEW YORK 19 • Chicago (2) 30 N. Michigan Ave.

PRINCIPLES AND PRACTICE OF

WAR SURGERY



by J. TRUETA, M.D.

Formerly Director of Surgery, General Hospital of Catalonia, University of Barcelona; Assistant Surgeon (E.M.S.) Wingfield-Morris Orthopaedic Hospital; Acting Surgeon-in-Charge, Accident Service, Radcliffe Infirmary, Oxford. 425 pages, 144 illustrations. PRICE, $6.50.

5-Point **TRUETA** *Technic*

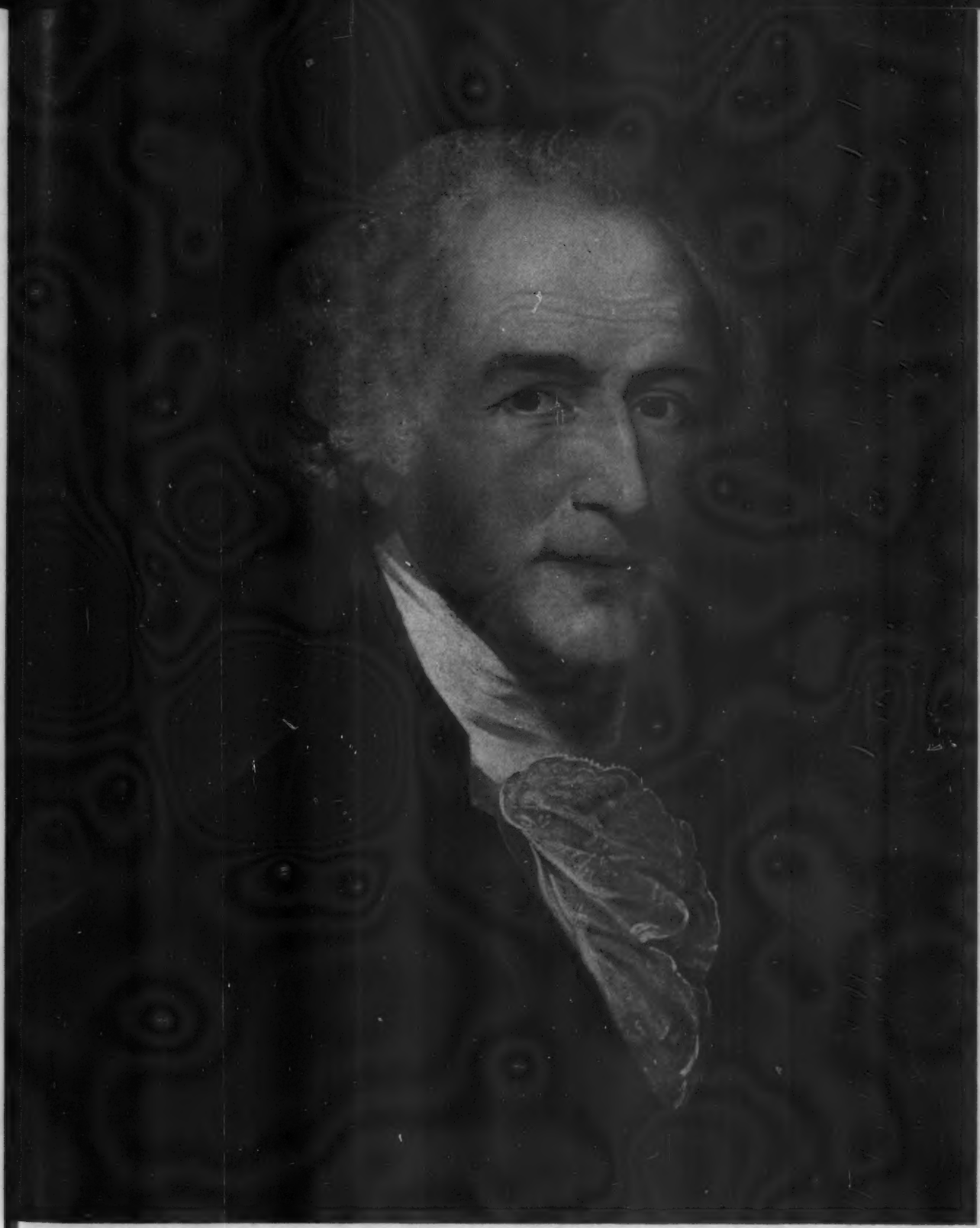
1. **Prompt surgical treatment.**
2. **Cleansing of the wound.**
3. **Excision of the wound.**
4. **Provision of drainage.**
5. **Immobilization in a plaster-of-Paris cast.**

Listed above are the five essential principles in the biological treatment of wounds as formulated by Trueta, each and every one of which must be applied to ensure the greatest possible success.

In this new book "PRINCIPLES AND PRACTICE OF WAR SURGERY," Trueta sets forth in complete detail these procedures which he has adopted as a result of his experience in the Spanish War and in World War II. However the book is not confined to these methods alone, but deals fully with such important subjects as shock, transfusion, aerobic and anaerobic infections, including gas gangrene and tetanus, chemotherapy, antiseptics, anesthesia, skin grafting, amputation, and treatment of burns.

Graphic illustrations such as those reproduced here supplement the text matter, supplying step-by-step visual guidance. You won't want to miss having this authoritative text. Send for it today!

THE C. V. MOSBY COMPANY, 3525 Pine Blvd., St. Louis 3, Mo.



ATTRIBUTED TO C. W. PEALE AFTER GILBERT STUART

COURTESY, SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA

William Shippen, M. D.

1736-1808

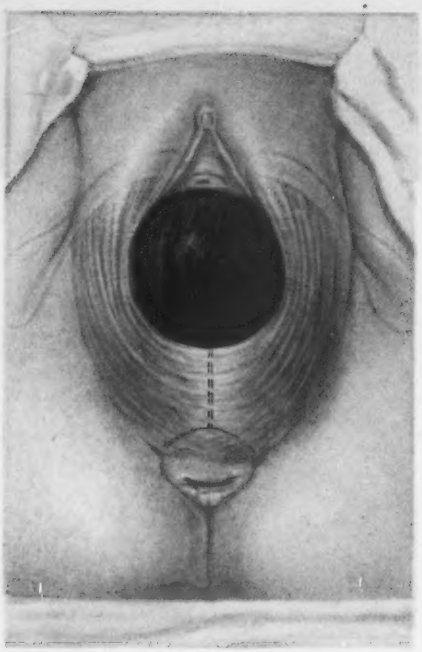
First Professor of Anatomy and Surgery in America (1762). With Dr. John Morgan, persuaded the Trustees of the College of Philadelphia to organize the medical department in 1765. Member of the Continental Congress. Chief Physician and Director-General of Hospitals of the Continental Army (1777-1781).

No. 6 in the series, Great American Surgeons. Reproductions suitable for framing sent free on request to:

ETHICON SUTURE LABORATORIES, DIVISION OF JOHNSON & JOHNSON, NEW BRUNSWICK, N. J.

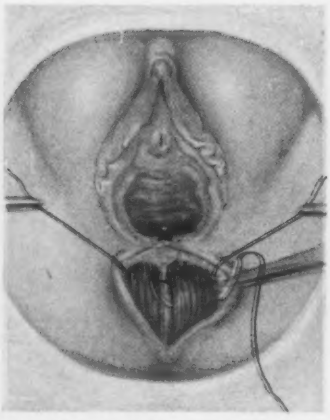
Median Episiotomy and Repair

(MATSNER)

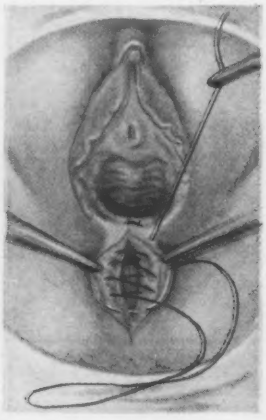


1. Vertical line indicates normal extent of incision. Arc line indicates elective extension, avoiding anal sphincters.

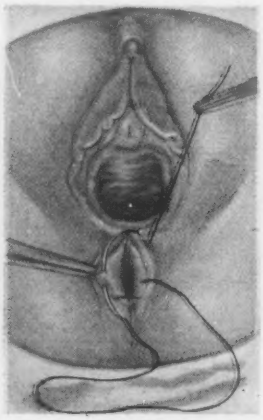
2. Incision is made in avascular midline area, separating the levator ani muscles. Tip-guard scissors used to avoid fetal trauma.



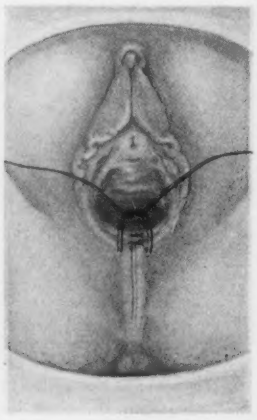
3. Vaginal mucous membrane sutured with interrupted chromic 00. Levator ani muscles approximated with interrupted chromic 0.



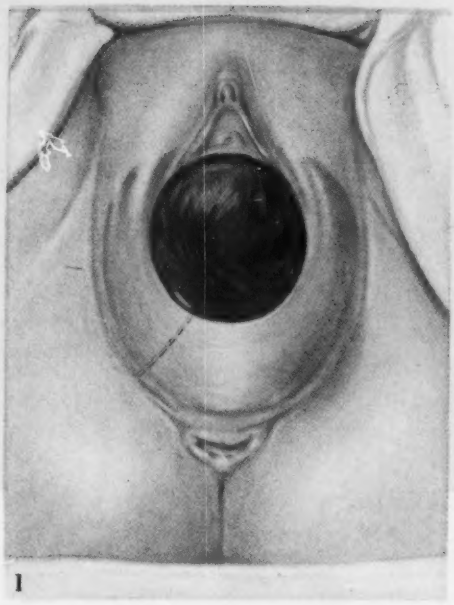
4. Continuous subcutaneous suture, chromic 00, beginning at upper angle and extending full length of incision.

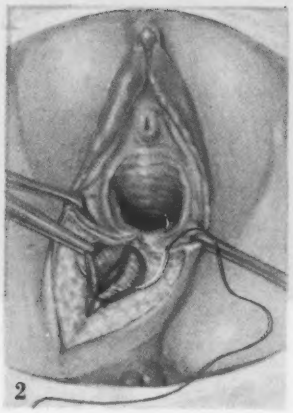


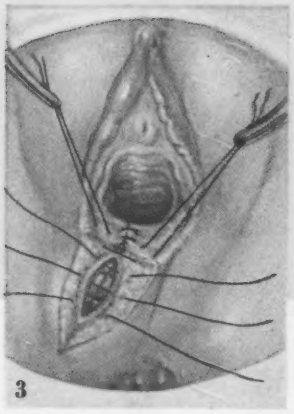
5. Same suture used for subcuticular closure beginning at base of incision and ending opposite primary introduction.



6. Subcutaneous subcuticular repair completed. Note plastic result and absence of irritating external sutures.


1


2


3

Mediolateral Episiotomy and Repair

1. Dotted line indicates usual extent and direction of incision which avoids possible extension into sphincter area. Incision can be made on either side.

2. Vaginal mucous membrane sutured with interrupted chromic 00. Deep interrupted chromic 0 sutures are used to approximate muscle.

3. Interrupted chromic 00 at mucocutaneous junction held by clamps until subcutaneous sutures are completed.

4. Skin closure completed by interrupted chromic 00. Note all suture ends are cut short to minimize irritation.

4

For Reduced Trauma...Less Tissue Reaction...Faster Healing
Use Ethicon Tru-Chromicized Fine Gauge Catgut Sutures

• The advantages of fine gauge suturing may be achieved with safety by using Ethicon Tru-chromicized, fine gauge catgut sutures. They possess a greater strength-diameter ratio than larger sizes; their gauge uniformity is 6 times greater than U. S. P. requirements; they retain their integrity longer than chromicized sutures of larger gauges.

Exceeding U. S. P. tensile strength requirements (averaging 20% or more on knot pull), Ethicon fine gauge sutures provide a substantial margin of safety against breakage.

ETHICON
Sutures

Surgical Gut with Lock-Knot Finish

Needle bending and breaking minimized

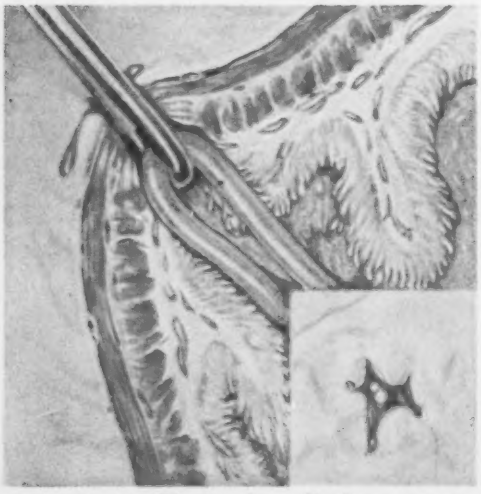
Atraloc Eyeless Needles facilitate surgical skill and dexterity with safety

Site where Atraloc needle may be safely held, permitting maximum bite and needle control.
Site where needles with softer steel shank must be held to avoid bending, breaking. Increases needle manipulation.

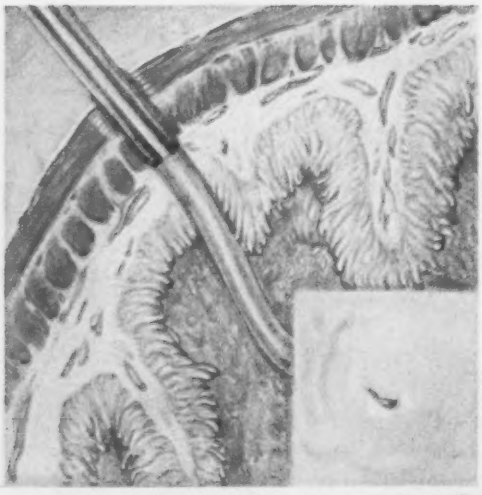
• The more highly tempered steel shank in Atraloc Eyeless Needles gives them greater strength and rigidity in use. A full bite can be taken with confidence when an Atraloc Needle is used to achieve tissue approximation. This greater efficiency eliminates extra manipulations and saves operating time, without increasing breaking hazards.

The shank of the Atraloc Needle is swaged to the suture by a special process. This process permits a relatively high temper just below the shank where strength counts most. Atraloc Needles hold on pulls in excess of U.S.P. tensile strength requirements for sutures pulled over a surgeon's knot.

ATRALOC NEEDLES for minimal suture trauma



EYED NEEDLE: The eyed needle does greater injury to tissue because it pulls a looped suture in its wake.



ATRALOC NEEDLE: The Atraloc Needle causes minimal injury. It pulls a single strand, slightly smaller than the needle.

ORDER FROM YOUR DEALER

ETHICON SUTURE LABORATORIES

Division of Johnson & Johnson *New Brunswick, N.J.*

World's Largest Manufacturer of Surgical Catgut

Suture Laboratories at New Brunswick, N. J.; Chicago, Ill.; Brazil; Argentina; England; Australia

Copyright 1944, Johnson & Johnson Printed in U. S. A.

VENUS DE MILO...art treasure without price! This remarkable statue, which is of heroic size, represents the perfect female figure...draped from the girdle to the feet. Both arms are missing. In beauty of execution and nobility of conception this epic work of sculpture stands without a rival in its portrayal of noble womanhood!

PERFECTION

in its field . . .

Just as the Venus de Milo is considered by many critics to be the most lovely example of ancient sculpture in the world today, so from the viewpoint of beauty, utility, long life and economy, surgical instruments and equipment bearing the name SKLAR stand for as near perfection as more than half a century of experience and skill can make them. All through the years . . . ever since it was founded...the J. Sklar Manufacturing Company has consistently maintained the highest standards of quality and workmanship. And this production policy plus unusual flexibility in adapting manufacturing processes to surgical trends has made SKLAR first choice with discriminating surgeons . . . the leader in a highly specialized industry. ***Sklar instruments are sold only through accredited surgical instrument distributors. A catalog of Sklar Stainless Steel Instruments will be provided on request.***

ARMY E NAVY

Sklar LONG ISLAND CITY, N. Y.

BABCOCK'S INTESTINAL FORCEPS, BOX LOCK, STAINLESS STEEL

LAWRENCE SHAW RIVALS THE F.B.I.

PHARMACIST LAWRENCE SHAW owns and operates a drug store in which professional service prevails. Mr. Shaw fills each prescription with meticulous care and with an exactness that approaches the point of fussiness. He is supported in his efforts by the assurance that the materials he uses in his compounding are the finest the markets of the world afford. Many of them come from the Lilly Laboratories, where quality has always been of first importance. Every safeguard known to man is employed in the manufacture of Lilly Products. Hundreds of people are employed in inspection alone. In providing medicinal agents made with such scrutinizing care, Pharmacist Shaw protects the lives of the people just as surely as do the sterling members of the F.B.I. ★ Eli Lilly and Company, Indianapolis 6, Indiana, U.S.A.

INVEST IN AMERICA'S FUTURE ★ BUY WAR BONDS

SURGERY

VOL. 16 DECEMBER, 1944 NO. 6

Original Communications

ESOPHAGEAL DUPLICATIONS OR MEDIASTINAL CYSTS OF ENTERIC ORIGIN

WILLIAM E. LADD, M.D.,* AND H. WILLIAM SCOTT, JR., M.D.†
BOSTON, MASS.

(From Department of Surgery, Harvard Medical School and Surgical Service, The Children's Hospital)

INTRODUCTION

IN THE last several years one of us (W. E. L.) has published reports concerning duplications of the alimentary tract and the surgical treatment of these "enterogenous cysts."[1, 2] During this time five individuals with enterogenous cysts of the mediastinum, or better, "duplications of the esophagus," have been treated at The Children's Hospital. The unique problems presented by these lesions and their surgical management have prompted this report.

CASE REPORTS‡

CASE 1 (No. 173795).—D. S., a white boy, 22 months of age, one of six children, was admitted to the Children's Hospital Feb. 20, 1928. The family and past histories were noncontributory. The child had been well until two months before entry at which time he developed pneumonia on the right side, with a high fever for four days. The temperature then returned to normal and after two weeks in bed the patient was allowed up. During his illness he lost considerable weight.

Four days before entry the patient became ill with fever, dyspnea, and vomiting. After the first day the fever subsided but the vomiting continued. On the morning of entry the right ear began to discharge purulent material.

Physical Examination.—Temperature was 101° F., pulse 130, respirations 40 to 50, weight 21 pounds. The child was a pale, underdeveloped, and undernourished boy who could lie only on his right side because of marked dyspnea. There was a harsh, brassy cough. A purulent otitis media was present on the right side.

*William E. Ladd Professor of Child Surgery, Harvard Medical School, Chief of Surgical Service, The Children's Hospital.

†Assistant in Surgery, Harvard Medical School and Junior Attending Surgeon, The Children's Hospital.

‡Cases 1 and 2 were reported previously by Mixter and Clifford[3] under the title of "Congenital Mediastinal Cysts of Gastrogenic and Bronchogenic Origin." Since we now know them to be duplications of the esophagus, we feel that it is justifiable to report these cases again with those of three more recent patients.

Received for publication, Oct. 11, 1944.

The chest was barrel-shaped with marked costal retraction and diminished expansion on the right side. The right base posteriorly was flat to percussion. Breath sounds were diminished over the whole right chest and absent below the angle of the scapula. A few moist râles were present over the right apex. Tactile fremitus was absent over the right side of the lower back with bronchial breathing over the right upper chest anteriorly. The heart was displaced 2½ cm. outside the left nipple line. The abdomen was protuberant and both spleen and liver were palpable 5 cm. below the costal margin. The fingers showed suggestive clubbing.

The roentgen examination suggested fluid, and a tentative diagnosis of empyema was made. Thoracentesis yielded 360 c.c. of a viscid, opalescent fluid. This was acid in reaction; its specific gravity 1.010; chloride 114 meq./1; bicarbonate 34 volume per cent; 560 cells per cubic millimeter with 80 per cent polymorphonuclears.

A.

Fig. 1 (Case 1, D. S.).—*A*, Sixteen years after successful operation for esophageal duplication. *B*, Roentgenogram of chest of same patient.

The withdrawal of the fluid afforded temporary relief of the symptoms. The diffuse clouding of the right chest by roentgenogram was replaced by a clear lateral lung field and a large, dense shadow running obliquely downward and outward from the hilus. Lipiodol bronchograms gave no diagnostic assistance, although the right upper bronchus failed to fill. The fluid rapidly reaccumulated and repeated tappings were necessary. The child continued to run a low-grade temperature. In view of the character of the fluid and the roentgenologic findings, a diagnosis of intrathoracic cyst was made.

Exploratory thoracotomy was carried out under gas-oxygen anesthesia on the twenty-second hospital day. The right upper lobe was atelectatic, rubbery, and yellowish red in color. The two lower lobes were only partially expanded and

displaced forward by a large, tense, smooth-walled cyst extending from the diaphragm to the apex of the thorax and filling the right paravertebral gutter. There were no adhesions within the pleural cavity. The cyst was estimated to fill two-thirds of the right thoracic cage. Anteriorly, it was covered by the visceral pleura which was reflected laterally onto the thoracic wall and mesially along the mediastinum, posterior to the root of the lung. In diameter it appeared to be about two and three-quarter inches at its diaphragmatic attachment,

B.

Fig. 1 *B. (For legend see opposite page.)*

which was retropleural. It was slightly smaller at the apical limit of the tumor, which was also covered by pleura. The condition of the child did not warrant excision of the cyst. Consequently its periphery was dissected free, the cyst wall sutured to the wound edges, and the chest wall closed around it in layers. Six days later the exteriorized cyst was opened and a catheter inserted for drainage. The latter procedure was followed by a very severe reaction with a high temperature. Four transfusions were given at intervals and there was gradual improvement. There were recurrent infections of the cyst cavity, however, with

elevation of temperature. There was no gain in weight, but the brassy cough ceased. Repeated roentgenograms with lipiodol injection into the marsupialized cyst demonstrated considerable diminution in size. There was a copious amount of clear, white, mucoid drainage which resembled gastric juice.

Four months after the marsupialization of the cyst an attempt at complete excision was carried out under gas-oxygen anesthesia. The old incision was reopened and the seventh rib resected. The cyst was found to be approximately one-half its former size. The wall was greatly thickened and fibrous. The condition of the three lobes of the lung remained the same as at the previous operation. The pleura was incised vertically over the surface of the cyst. No cleavage plane could be found. In consequence, the cyst was freely opened and with a finger introduced into its cavity it was excised to its base by sharp dissection, including the overlying pleura which could not be detached. The medial wall was intimately adherent to the esophagus along the latter's central two-thirds and this long narrow base of the cyst could not be excised completely. However, the mucosal surface of the base was stripped off and two gauze packs placed against the remaining base and led out through either extremity of the thoracotomy wound. There was relatively little hemorrhage. The wound was then approximated closely about the packs.

The child's condition was precarious at the end of the operation. After intravenous glucose followed by transfusion his condition improved and he subsequently made a satisfactory convalescence. The gauze drains were removed on the tenth postoperative day following which the sinuses gradually granulated in without infection and the wound was entirely healed by the end of a month. This boy has been followed for sixteen years since his discharge from the hospital and has developed normally with only slight residual weakness of the right shoulder as a result of operative obliteration of the esophageal duplication. (See photograph and x-ray picture of chest, Fig. 1.)

Pathologic Examination.—Examination of the cyst wall showed it to have the histologic characteristics of stomach wall. There was a typical gastric mucosa containing chief and parietal cells with an underlying muscularis mucosa, submucosa, and muscularis. Rugae were present in some areas with strands of smooth muscle as seen in the normal stomach wall. The mucosa was destroyed in areas with fibrous tissue replacement and scattered throughout there were areas of hemorrhage and cellular infiltration.

Diagnosis.—Esophageal duplication lined by gastric mucosa.

CASE 2 (No. 118048).—J. B., a white, male infant, was admitted to the hospital Sept. 14, 1927, at the age of 7 weeks, because of feeding difficulties and failure to gain.

The family history was negative. The birth weight was 9¾ pounds. The neonatal period was uneventful except for paroxysms of pain when nursing. These were characterized by doubling up of the legs and screaming, with some regurgitation of feedings. A small amount of dark blood was vomited on one occasion. For several days he had been coughing frequently.

Physical Examination.—Examination revealed a pale, undernourished infant with rapid labored respirations. Temperature was 100.6° F. Further examination revealed head, eyes, ears, nose, and throat, negative; heart and lungs, not remarkable on admission except for slight dullness and a few scattered râles over the right apex posteriorly. abdomen, nontender with no masses; rectal, reflexes, and extremities, negative.

Laboratory work showed a red blood count of 3,600,000, hemoglobin 60 per cent, white blood count 21,500 with 74 per cent polymorphonuclears. Wassermann was negative. Tuberculin was negative in dilution 1:25.

Roentgenograms of the chest showed a diffuse hazy infiltration of the entire right upper lobe.

The infant had a febrile course with increasing respiratory difficulty. Regurgitation of feedings persisted but barium studies showed no obstruction or displacement of the esophagus and no abnormality of the gastrointestinal tract. After several weeks he developed dullness over the whole right side of the chest with diminished breath sounds over the upper lobe. Repeat roentgenograms of the chest showed almost complete opacity of the right lung field with some mediastinal displacement to the left side. An area of pressure erosion was identified in the region of the angles of the fourth and fifth ribs posteriorly. Thoracentesis was carried out in this area and 10 c.c. of thick, viscid, mucoid fluid was aspirated under considerable pressure. This contained 700 cells per cu. mm., mostly red cells with a moderate number of lymphocytes. Smear and culture revealed no organisms. No hairs or epithelial cells were encountered. The following day a second tap was performed and after aspiration of 35 c.c. of the same type of fluid 10 c.c. of lipiodol were injected. Roentgenograms of the chest at this time showed a large cystic tumor of the posterior mediastinum extending toward the apex of the right lung and displacing both esophagus and trachea anteriorly.

Exploratory thoracotomy was carried out under gas-oxygen anesthesia, the mediastinum being entered extrapleurally through the beds of the resected posterior segments of the third and fourth ribs. Because of respiratory difficulties an adequate exploration could not be performed and the child was returned to his bed in a precarious condition. Four weeks later a second attempt was made and again the cyst could not be located, hurried exploration being necessary because of the child's poor condition. After an extremely stormy postoperative period characterized by recurrent bouts of bronchopneumonia the patient was discharged to a convalescent home.

At the age of 1 year the baby was readmitted in the hope that surgical approach to the cyst might be more successful. The general symptoms were unchanged. His weight at this time was 11 pounds. There was dullness and breath sounds were absent over the entire right upper chest with numerous râles over the right lower lobe and the entire left lung field. Fingers were definitely clubbed.

Several thoracenteses failed to enter the cyst. Recurrent exacerbations of chronic pneumonia prevented further surgical exploration. The patient finally succumbed to severe bronchopneumonia at the age of 16 months weighing at that time 10½ pounds.

Autopsy.—Autopsy revealed a 5 cm. cystic mass lying in the right paravertebral gutter adjacent to the esophagus and attached to the posterior chest wall and pleura over the right apex. The cyst was retropleural and had eroded the bodies of the upper thoracic vertebrae as well as the adjacent ribs. There was diffuse interstitial pneumonia, both acute and chronic.

Gross examination of the cyst showed it to resemble a portion of the gastrointestinal tract. There was a pleural reflexion resembling a serosa, a two-layered muscularis, a definite submucosa and a thick velvety mucosal lining which was thrown into numerous folds similar to gastric rugae. The cyst was not attached to the esophagus, trachea, or bronchi.

Microscopic examination revealed a typical gastric mucosa with deep branching glands lined by chief and parietal cells.

Diagnosis.—Esophageal duplication lined by gastric mucosa.

CASE 3 (No. 211576).—N. C., a 7-month-old girl, was admitted to the Children's Hospital, April 22, 1937, with a complaint of intermittent abdominal cramps of six months' duration.

Family history was irrelevant. Past history showed that the baby was delivered normally at full term, weighing 7½ pounds. The neonatal period was uneventful. She took feedings well and made a steady weight gain, reaching 13 pounds at six months. Since the first month of life the infant had been subject to occasional bouts of "abdominal cramps," which doubled her up and caused her to scream. In the six weeks prior to entry she had had these episodes four to five times per week and had developed anorexia with failure to gain. Ten days before admission she developed a dry cough, accompanied by fever and transitory cyanosis. Since that time she had refused to lie on her right side and had persistent respiratory distress, cough, and temperature ranging between 100 to 103° F. Vomiting of feedings occurred two to three times daily. Stools remained essentially normal without blood. There was no hematemesis or hemoptysis.

Physical Examination.—Examination on admission revealed a fairly well-developed, somewhat undernourished 7-month-old baby girl with slight cyanosis, breathing with difficulty. Examination of head, eyes, ears, nose, and throat was negative. The neck was short and the thoracic cage asymmetrical, there being a diffuse bulging of the right side of the chest posteriorly. The respiratory excursion was diminished on the right side. On percussion there was flatness over the right lung posteriorly with hyper-resonance anteriorly. Breath sounds were diminished on the right side posteriorly. There was questionable shift of the heart and mediastinum to the left. The heart was not enlarged, and there were regular rhythm, sounds of good quality, and no murmurs. The abdomen was soft and relaxed with no tenderness, spasm, or masses. The liver edge was palpable two fingers below the costal border. Examination of the genitals, rectum, reflexes, and extremities was essentially normal.

Laboratory work on admission showed a white blood count of 18,000 with 76 per cent polymorphonuclear leucocytes. Red blood count was 4,880,000 with 75 per cent hemoglobin. Urinalysis was negative. The blood Hinton test was negative.

Roentgenograms of the chest showed a large spherical mass about 8 cm. in diameter filling most of the right hemithorax and displacing the heart to the left. Fluoroscopy of the esophagus showed it to be displaced to the left in its lower third by the mass (Fig. 2).

Course.—A few days after admission, mediastinal exploration was carried out under cyclopropane anesthesia. A transpleural approach through a right posterolateral thoracotomy with resection of a segment of the seventh rib revealed an orange-sized cystic mass occupying the lower third of the right hemithorax. The cyst was retropleural in location and had a sessile attachment to the lower third of the esophagus. After freeing the periphery of the mass from the mediastinal pleura, marsupialization of the cyst was carried out by first aspirating its contents (about four ounces of brownish serous fluid) and then suturing the wall of the cyst to the wound edges with interrupted silk sutures. The chest was then closed in layers to the marsupialized cyst, following which a circular segment was excised from the exteriorized cyst wall and a rough gauze pack inserted into the cavity.

The postoperative course was uneventful. The marsupialized cyst drained copious amounts of watery fluid which had an acid reaction. Barium swallows showed no lumenal connection between the esophagus and the cyst.

Fifteen days after marsupialization, excision of the cyst was undertaken under cyclopropane anesthesia. The marsupialized segment of the cyst was dissected free from the wound edges, the old thoracotomy wound opened, and dissection in the region of the attachment of the cyst showed the latter to be connected to the right side of the esophagus at the junction of its middle and lower thirds. No cleavage plane could be found and there seemed to be a common muscularis. Accordingly, the base of the cyst was cut across and the cyst removed

leaving a defect measuring about 3 by 2 cm. in size in the esophageal wall. The esophageal defect was closed by bringing the submucosa and muscularis together with a continuous suture of fine silk. The chest was closed with drainage of the pleural cavity.

The patient's postoperative course was stormy and on the third postoperative day the esophageal suture line broke down with the establishment of an esophagopleural fistula. Consequently, two days later, the chest was reopened in an attempt to close the fistula. The child did poorly during the operation, however, and a hurried closure of the esophageal defect was carried out with interrupted fine chromic catgut mattress sutures to submucosa and muscularis in two

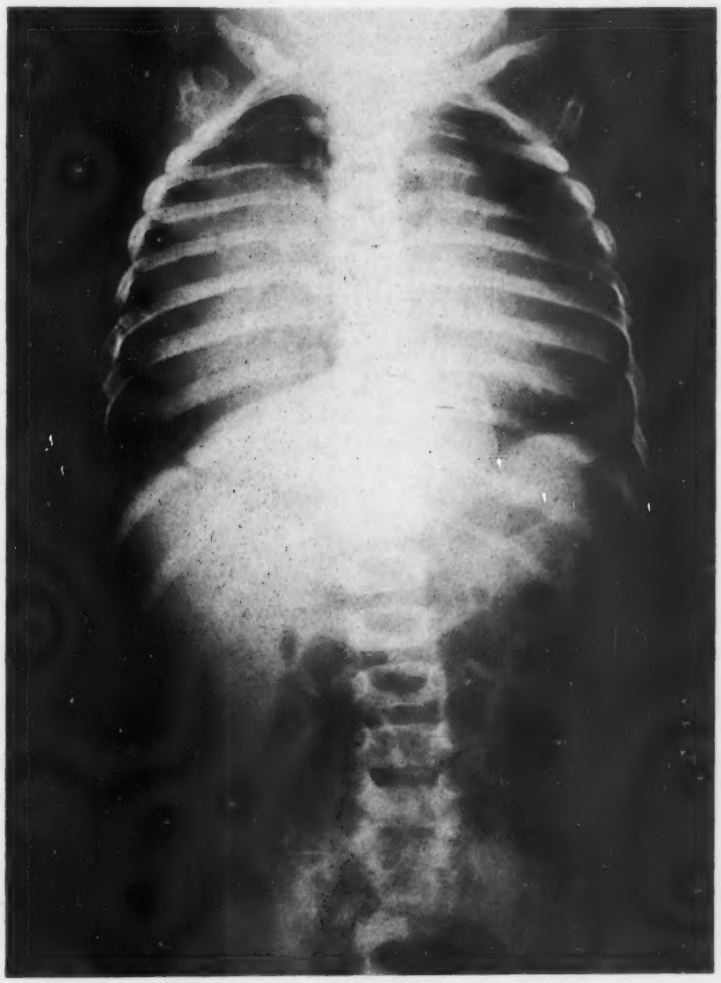


Fig. 2 (Case 3, N. C.).—Note large esophageal duplication filling two-thirds of right hemithorax.

rows. Again, the chest was closed with drainage. About one week postoperatively saliva and curds appeared on the dressings despite the fact that the child had been maintained on gastric feedings via a Levin tube. The re-established esophagopleural fistula soon began to drain copious amounts of saliva, amounting to eight to ten ounces daily.

A gastrostomy was performed, but despite carefully regulated feedings the child's nutrition was maintained with difficulty because of frequent episodes of diarrhea, vomiting, and recurrent bouts of pneumonia.

About one year after the last attempted closure of the esophageal defect, the chest sinus completely closed over, but fluoroscopic study of the esophagus with barium revealed the persistence of a fistulous tract connecting the esophageal lumen and a cystic mediastinal cavity. Consequently, a second attempt at closure of the esophageal fistula was carried out by the transpleural route. Because of multiple adhesions, dissection was difficult. A lemon-sized sac was encountered in the right side of the posterior mediastinum. This was dissected free with considerable difficulty and was found to be attached to the esophagus by a narrow 3 cm. fistulous tract measuring about one inch in diameter. This tract was freed, clamped, and divided close to the esophagus, leaving a defect in the wall of the latter about one inch in diameter. The defect was closed by approximating mucosa with interrupted fine silk, muscularis with mattress sutures of the same material, and finally bringing adjacent pleura over the suture line with a continuous suture. At this point in the procedure the child's respirations became shallow and irregular, and complete excision of the sac could not be performed—instead, it was partially excised and the remainder marsupialized into the thoracotomy wound, packed with rough gauze, and the chest wall closed.

Four days after this procedure the esophageal suture line broke down and the fistula was re-established. Copious amounts of saliva were drained from the child's chest wound. Two months after this last attempted closure she developed a severe diarrhea associated with interstitial pneumonia and died at the age of 1 year, 11 months, thus ending a fifteen months' hospital stay.

Pathologic Findings.—The surgically excised cyst measured 5 by 6 cm. Its external surface was covered by a serous capsule (pleura) through which the muscular wall appeared pale gray in color. There were two distinct muscular lamellae, each about 2 mm. thick, and on the inner surface a smooth, mucosal lining, yellowish red in color with large rugae and measuring from 1 to 2 mm. in thickness. Microscopic examination revealed the mucosa to be of gastric type. There were large branching glands of mucus-secreting cells with smaller deeper cords of glands lined by parietal and chief cells. The submucosa was a well-defined structure without inflammatory infiltration. Two layers of smooth muscle constituted the muscularis.

Diagnosis.—Duplication of esophagus lined by gastric mucosa.

Autopsy.—Examination revealed a fistulous tract extending from the lower third of the esophagus through the right posterior pleural cavity to the chest wall. There were extensive fibrous pleural adhesions adjacent to the fistula, but there was no empyema. The right lower lobe of lung contained large areas of fibrosis. In addition there were multiple areas of lobular atelectasis and diffuse interstitial pneumonia, both acute and chronic, involving all lobes of both lungs. Aside from signs of malnutrition, there were no other significant findings.

CASE 4 (No. 257878).—P. H., a 3-week-old boy, was admitted to the Surgical Service of The Children's Hospital because of a mediastinal mass discovered roentgenologically in a film of the spine taken in the routine orthopedic work-up of clubfeet. Birth was at full term, with normal delivery, and uneventful neonatal period. The baby weighed 9 pounds at birth, took breast feedings well, and gained to 10 pounds at the time of admission. Bilateral talipes equinovarus noted at birth had brought the infant to the orthopedic outpatient department. The mediastinal mass discovered by roentgenogram had apparently caused no symptoms whatever. There was no respiratory distress, cough, cyanosis, hemoptysis, feeding difficulty, pain, or vomiting.

Physical Examination.—Examination on admission showed a well-developed and well-nourished male infant, in no distress. Color and hydration were good. Examination of head, eyes, ears, nose, and throat was negative. The trachea deviated about 1 cm. to the right of the midline at the suprasternal notch. The heart was

not enlarged, but the border on the right side of the heart was percussed about 2 cm. to the right of the sternum. The apical impulse was palpable at the left sternal border in the fourth interspace. Heart sounds were of good quality and there were no murmurs. The lungs were clear to auscultation and percussion. No areas of dullness could be made out. There were no râles. The abdomen was soft and nontender with no palpable organs or masses. Genitals, rectum, and reflexes were found to be normal on examination. There was bilateral talipes equinovarus, more marked on the left side.

Laboratory work on admission showed negative urinalysis, red blood count 4,940,000, hemoglobin 80 per cent, white blood count 9,700 with a normal smear. Blood Hinton test was negative.

Roentgenograms of the chest showed the heart and mediastinum to be displaced to the right by a large, 5 cm., rounded, well-circumscribed soft tissue mass in the posterior mediastinum, situated behind the heart and extending out into the left hemithorax. Fluoroscopic examination of the esophagus with barium showed that the esophagus was displaced forward and to the right by the mass.

Course.—Shortly after admission mediastinal exploration was carried out under cyclopropane anesthesia. The chest was entered through a left posterolateral thoracotomy, resecting the posterior segments of the eighth and ninth ribs subperiosteally. Upon opening the pleura a soft, yellowish-gray, cystic mass was noted in the lower third of the thorax. This was retropleural in location, measured about 5 cm. in diameter, and was roughly spherical. Dissection readily freed the periphery of the cyst from the overlying pleura and it was found to be attached by a pedicle about 1.5 cm. wide to the left wall of the esophagus at the junction of the latter's middle and lower thirds. The cyst was then grasped with Allis forceps, drawn into the thoracotomy wound, and sutured to the pleura and intercostal muscle with interrupted 6-0 silk. The chest wall was then closed in layers with silk to the marsupialized cyst, following which the exteriorized cyst wall was incised with the escape of three to four ounces of watery, blood-tinged fluid. Biopsy was done on a segment of the wall and the margins of the marsupialized cyst were sutured to skin edges with interrupted 6-0 silk sutures. The cyst's cavity was then packed firmly with gauze.

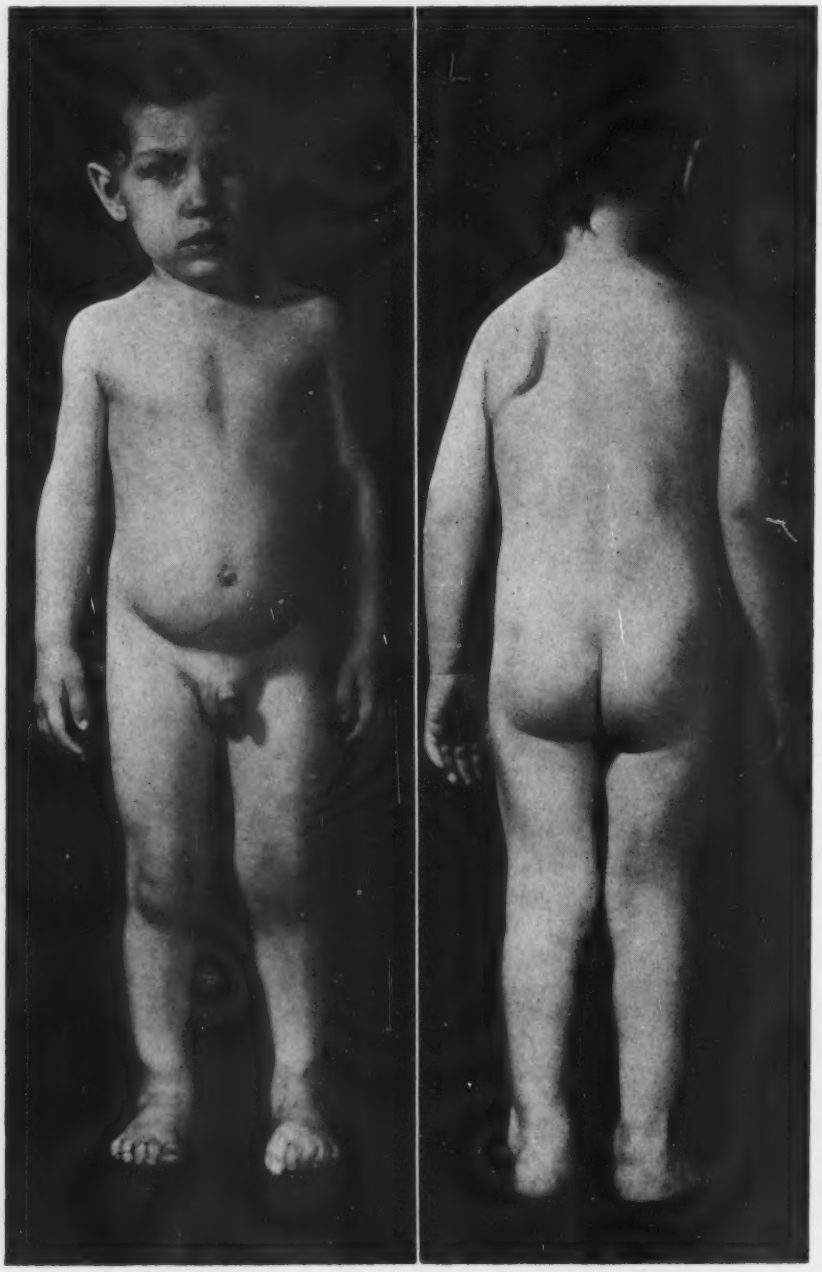
The baby's postoperative course was satisfactory. The exteriorized cyst drained moderate amounts of clear fluid which had an acid reaction. The gauze packing was changed frequently at first. Feedings were taken well by mouth, and there was no evidence of a connection between the esophageal lumen and that of the cyst by clinical observation or by lipiodol injection.

About one month after the original operation, the lining membrane of the marsupialized cyst was curetted thoroughly, snugly packed with gauze, and the pack left in place for one week. Following this procedure the discharge from the sinus steadily decreased. The child was discharged home two months after entry and follow-up was carried on in the outpatient department. The sinus continued to discharge small amounts of serous fluid, necessitating daily dressings. The baby's general condition remained excellent and he gained well.

Nine months after the original operation the baby was readmitted because of persistence of discharge from the chest sinus and curettage was again carried out. At this time pathologic study of the curettings failed to show any mucosa but only granulation tissue and fibrinopurulent exudate. After a curettage of the lining membrane a gauze pack was again inserted. Postoperatively the discharge diminished temporarily, but soon became fairly profuse again. Consequently, one month later a secondary marsupialization of the cyst was performed under cyclopropane anesthesia. The cyst wall was dissected free down to the esophagus, mobilizing the former adequately to allow excision of a cuff of distal cyst wall about 3 cm. long. The cavity was again thoroughly curetted, treated with 95 per

cent alcohol, and repacked with gauze. Postoperatively, the baby did well, and the sinus gradually filled in with granulation tissue, being solidly healed in a month.

Follow-up has been continued for three and one-half years and there has been no subsequent evidence of recurrence of the cyst by clinical or roentgenographic observations. The patient has developed normally and has no symptoms relative to his esophageal duplication (Fig. 3).



A. *B.*

Fig. 3 (Case 4, P. H.).—Aged 2-10/12 years. Two and one-half years following treatment of esophageal duplication.

Pathologic Findings.—The segment of the wall of the cyst showed it to be about 4 mm. thick. The pleura was reflected over and adherent to the outer surface resembling a serosa. The inner surface was lined by a pale, yellowish mucosa with definite rugae. Microscopic sections of the wall of the sac showed it to consist of a double layer of smooth muscle, a submucosa, muscularis mucosae, and a well-developed mucosa. The mucosa was characterized by fairly deep branching glands, lined by mucous cells near the surface, whereas the lower portions of the glands contained chief and parietal cells. The entire picture was characteristic of gastric mucosa. No abnormalities of the structure of the wall or of the mucosa were noted.

Diagnosis.—Duplication of esophagus lined by gastric mucosa.

CASE 5 (No. 273768).—E. B., a 2-year-old boy, was first admitted to the Infants' Hospital at the age of 1 year because of hemoptysis of three days' duration. Family history was noncontributory. Past history showed that the child was delivered normally at full term, weighing 7 pounds, with an uneventful neonatal period. The baby had been well until one week before admission when he developed an upper respiratory infection with coryza, cough, and low-grade fever. In the three days prior to admission the patient coughed or "spit up" bright and dark blood in small amounts on several occasions.

Physical Examination.—Examination on admission showed a poorly nourished, underdeveloped, pale boy with slightly labored respirations. Temperature was 99.6° F.; pulse, 172; respirations, 32; weight, 15 pounds. Examination of head, eyes, ears, nose, and throat was negative. The chest was symmetrical and the lungs were resonant throughout. Breath sounds were vesicular with a few scattered, coarse râles over the right base posteriorly. Heart was within normal limits. Abdomen, genitals, rectal, extremities, and reflexes were not remarkable.

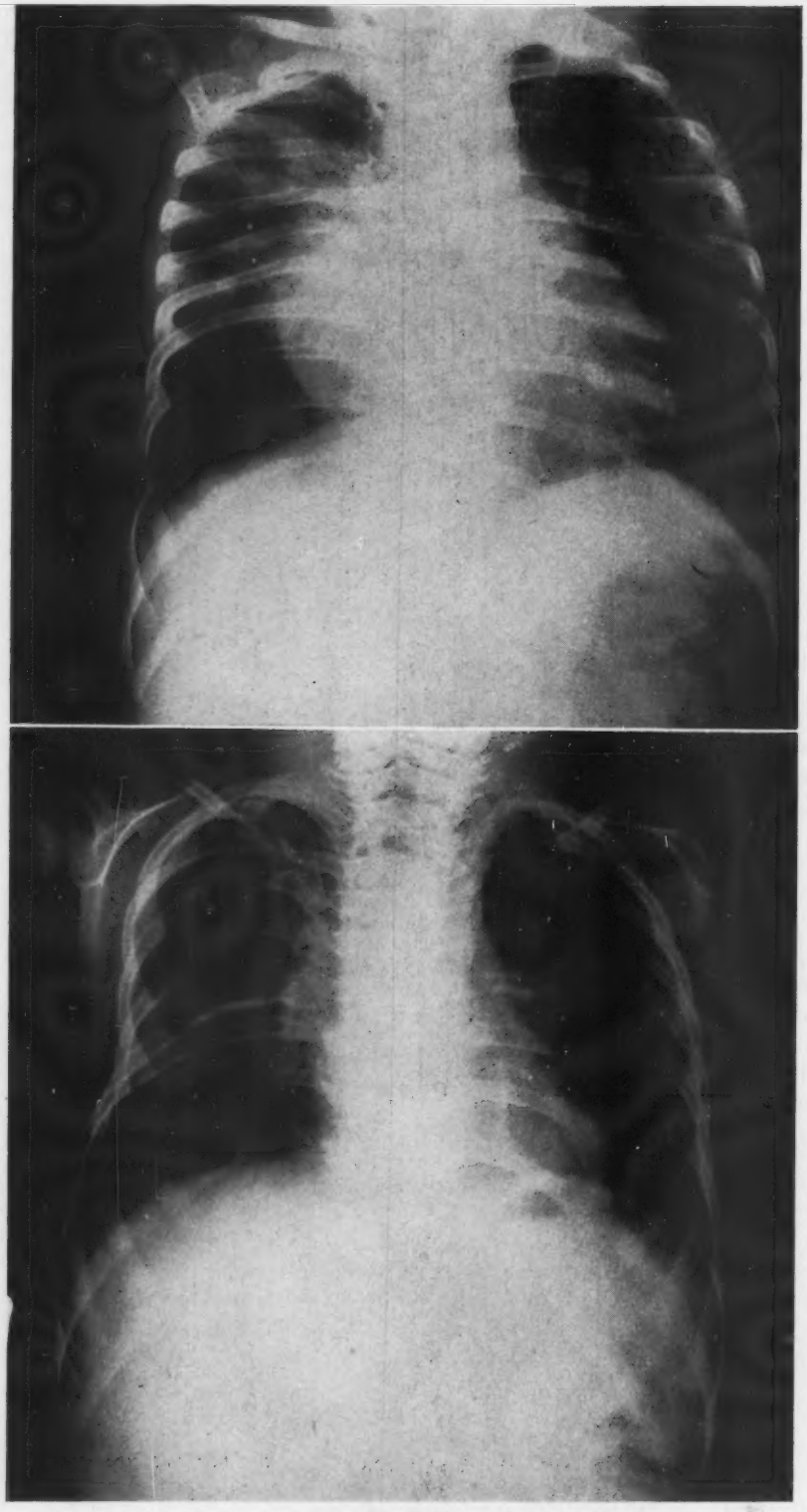
Laboratory work on admission showed negative urinalysis, red blood count 3,350,000, with hemoglobin 40 per cent. White blood count was 39,900 with 61 per cent polymorphonuclears and marked hypochromia of red cells on smear. Tuberculin was negative in dilution 1:100. Stool showed ++++ guaiac test. Bleeding, clotting, and prothrombin times were within the normal range.

Course.—Roentgenogram and fluoroscopic examination of the chest showed rather dense infiltration of the medial third of the right lung, more marked in the right lower lobe. In addition, there was a rounded, circumscribed, soft tissue mass about the size of an orange lying in the central portion of the posterior mediastinum on the right. This caused no cardiac displacement (Fig. 4). Bronschoscopy with lipiodol bronchograms was next carried out showing no bleeding point or ulceration in the tracheobronchial tree. There was some downward displacement of the right lower lobe bronchus by the posterior mediastinal mass but bronchograms were otherwise negative. Barium fluoroscopy of the esophagus showed no distortion or encroachment upon the latter by the mediastinal mass. An esophagoscopy showed no varices, ulcerations, or any other source of bleeding. Gastrointestinal series was negative.

During this period of studies the baby had a low-grade fever, cough, and several episodes of coughing or "spitting up" blood. It could never be conclusively decided as to whether he had hemoptysis or hematemesis. He was maintained on sulfadiazine and given several small transfusions.

Mediastinal exploration was decided upon after consultation between medical, surgical, and roentgenologic services. Diagnoses which were entertained included mediastinal tumor, mediastinal effusion or empyema, and esophageal duplication. Consequently, on the eighteenth hospital day mediastinal exploration was carried out through a right posterior thoracotomy under cyclopropane anesthesia. Posterior segments of the fourth and fifth ribs were resected subperiosteally. The

A.



B.

Fig. 4 (Case 5, E. B.).—Chest roentgenograms before first operation (*A*) and two months after second operation (*B*).

pleura was stripped down off the rib necks and the vertebral bodies in an extrapleural approach to the mediastinal mass. This was only partially successful, however, as the pleura was inadvertently opened and the underlying lung appeared to be rubbery hard in consistency and densely adherent to a poorly circumscribed extrapleural mass which filled the right paravertebral gutter. The pleural defect was then closed and extrapleural dissection into the mediastinum revealed an extremely vascular mass of adherent inflammatory tissue which contained old clotted blood in its midst. No cleavage planes could be found around this mass. The esophagus could not be identified. No cyst, discrete tumor, or fluid collection was encountered. As the center of the mass was broken into there was a very brisk hemorrhage which could be checked only by tight packing. The child's condition at this point became critical despite transfusion, and further investigation of the mass was out of the question. Consequently, the wound was rapidly closed in layers around the pack which was left in place and led out through the lower angle of the incision.

The immediate postoperative period was extremely stormy. Bleeding from the mediastinal mass continued at an alarming rate necessitating frequent changes of pack and multiple transfusions. The baby developed considerable pneumonitis with pleural effusion and also a *Staphylococcus aureus* wound infection, undoubtedly related to the repeated packings which were necessary to control the persistent bleeding from the mediastinal lesion. Sulfadiazine was administered in full doses. Three weeks after the first operation a second procedure was carried out under local anesthesia in an effort to obtain a biopsy of the mediastinal mass and to stop the persistent hemorrhage. Again, the child's precarious condition prevented anything more than biopsy and tight packing of the profusely bleeding sinus leading into the posterior mediastinum.

The biopsy showed only granulation tissue and no satisfactory diagnosis could be made. Repeated chest pictures offered no clue as to the nature of the lesion. On the basis that we might have been dealing with hemangioma or a malignant neoplasm which had possibly eroded the wall of one of the great vessels, a course of roentgen therapy was given (a total of 2,100 r. over the chest and back).

Two months after the first operation the bleeding tendency stopped and the wound could finally be left open without packing. It slowly granulated in and was solidly healed in another month. During this period the child's nutrition and general health improved markedly. X-ray pictures of the chest showed the posterior mediastinal mass to be smaller but still present. There were no subsequent episodes of hematemesis or hemoptysis.

The child was sent to the convalescent home for several weeks and continued to improve in nutrition. However, a follow-up chest roentgenogram at this time showed a definite destructive lesion of the bodies of the sixth and seventh thoracic vertebrae consistent with osteomyelitis. Consequently, he was readmitted to the hospital at the age of 17 months. Examination at this time showed slight dorsal kyphosis. There was a tiny sinus at the bottom of the old depressed thoracotomy scar which drained small amounts of seropurulent material culturing *Staphylococcus aureus.* The baby was immobilized in hyperextension on a Bradford frame for two months and then placed in a plaster shell. The sinus healed completely and roentgenograms showed healing of the osteomyelitis. One episode of hemoptysis occurred when he was 19 months of age. Chest roentgenograms at the time showed the mediastinal mass to be even smaller, and gastrointestinal series was negative.

Once more the child was sent to the convalescent home in his plaster shell and remained essentially asymptomatic for two and one-half months when small amounts of dark blood were noted to be draining from the small thoracotomy sinus which had re-opened.

He was re-admitted to the hospital and examination of the chest wound was essentially as before excepting that the edges of the tiny sinus appeared to be macerated. Black, changed blood was draining from the opening in small quantities. A few days after admission a few drops of clear fluid appeared in the sinus opening (Fig. 5). This had a pH of 4.0. Repeated specimens were collected for chemical analysis showing acidity ranging constantly between pH 3.5 and 4.5, definite peptic and rennin activity. Chloride was 120 meq./l with sodium 89 meq./l. Roentgenograms with lipiodol instillation into the sinus by means of a ureteral catheter showed a narrow tract about 3 to 4 cm. long extending to a cystic cavity about the size of a walnut in the right paravertebral gutter opposite the sixth dorsal vertebra. Barium fluoroscopy of the esophagus at the same time showed no displacement or abnormality of the latter's contour, although the cyst lay close beside it.

Fig. 5 (Case 5, E. B.).—Photograph of back ten months after first operation showing sinus discharging "gastric juice."

Finally a definite diagnosis became apparent: esophageal duplication lined by gastric mucous membrane. The child was operated on again (approximately one year after his original hospital entry); under cyclopropane anesthesia the sinus tract was first dilated and curetted and then dissected out down to the extrapleural cystic cavity. Upon excising the sinus tract the fundus of the little cyst could be visualized directly. It was thoroughly curetted in an effort to remove all mucosa down to the gristly muscular wall. The wall was then treated with tincture of iodine and the cavity tightly packed with about seven feet of three-quarter inch iodoform gauze. This was left in place for ten days and then re-

moved and the cavity allowed to granulate in. Healing was complete in four weeks with no further discharge to suggest residual mucosal lining. At the time of this report, the osteomyelitis of the vertebrae remains quiescent and seems satisfactorily healed. The child is still under observation but will be discharged home shortly.

Pathologic Report.—Examination of the cyst wall and curettings showed a mucous membrane which was histologically identical with gastric mucosa and entirely consistent with esophageal duplication lined by a gastric type of mucosa (Fig. 6).

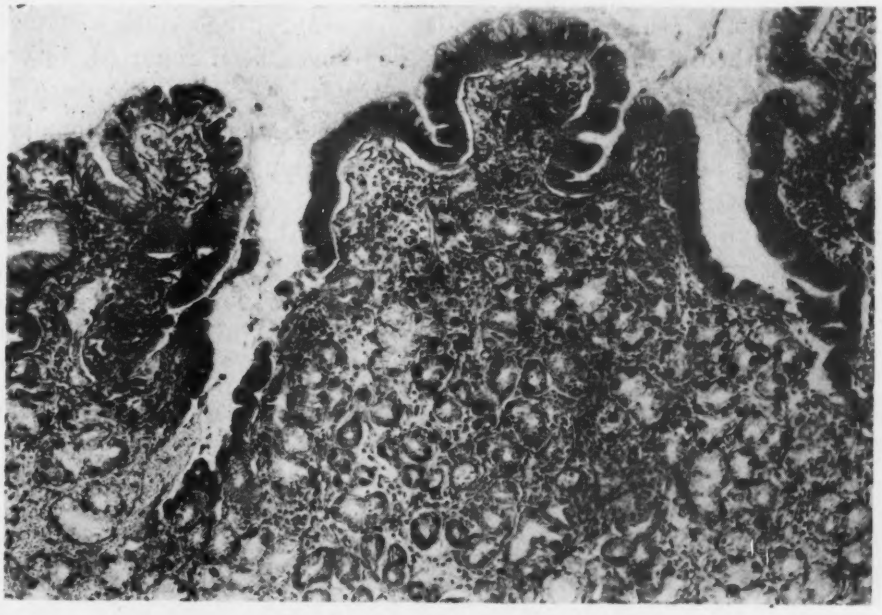


Fig. 6 (Case 5, E. B.).—Photomicrograph of lining of esophageal duplication in Case 5. Note typical gastric mucosa.

PATHOLOGY

Esophageal duplications are cystic structures of variable size possessing thick walls and a mucous membrane lining. They arise in the posterior mediastinum and usually expand into the right or left hemithorax, remaining retropleural in location. The cysts have been encountered along the entire length of the mediastinum but are most common in the middle third.

Histologically, the duplications usually have a two-layered muscular wall resembling esophagus. The mucosa, however, does not necessarily correspond to that of esophagus, but may closely simulate gastric mucosa. Some of the cysts have elements of both esophageal and gastric mucous membranes. A true serosa is absent, although the pleura is occasionally reflected over the larger cysts so as to resemble grossly a serosal coat.

Perhaps the most significant fact from a surgical viewpoint regard- their histology is the frequency of an intimate attachment to the esophagus. The muscular coats are usually densely adherent to those

of the esophagus and, indeed, there may be a common muscularis between the two structures. A few of the duplications have been found to have no attachment whatsoever to the esophagus.

One of our cases falls into the latter group, while in three patients the duplications were attached to the esophageal wall with no intervening plane of cleavage. In one individual the cyst's attachment could not be determined at operation. None of the duplications in our series had a fistulous communication with the esophageal lumen as occasionally found in duplications of the intestine. Such a connection is a theoretical possibility but has never been reported, to our knowledge.

The contents of the cysts usually resemble gastric juice. In our last patient the fluid gave positive tests for rennin and pepsin. As the acid-secreting elements of gastric mucosa are frequently present, high titers of hydrochloric acid may be encountered. One case is reported in the literature[4] of peptic ulcer developing in an esophageal duplication and giving rise to a fatal issue by perforating into the pleural cavity and lung. Peptic ulceration best explains the changes found at the first operation in Case 5 in our series.

The cysts vary considerably in size. Our largest specimen filled two-thirds of the right thoracic cavity in a 22-month-old boy. The others averaged about 5 cm. in diameter. Four of our patients had a typical gastric type of mucosa, while the other presented a lining membrane resembling esophageal mucosa in some areas, gastric in others, and duodenal in still other sections.

EMBRYOLOGY

Numerous theories have been proposed in an attempt to explain the occurrence of alimentary duplications in general.[1, 2, 4, 5] Those occurring along the course of the small bowel were formerly thought to be related in some fashion to Meckel's diverticulum. Twinning affecting only a portion of the alimentary tube has been advanced as a possible explanation, but proof of such occurrence is lacking.

Lewis and Thyng[6] found diverticula frequently in the fetal alimentary tract of pigs, rabbits, cats, sheep, and man. According to these authors, such diverticula normally regress, but persistence or sequestration of a "knoblike outpocketing of intestinal epithelium" might give rise to an adjacent duplication either separate from or connected with the alimentary wall or lumen. However, diverticula resembling those described in fetuses by Lewis and Thyng are extremely rare in early postnatal life. The clinical evidence also fails to suggest their theory. The fetal diverticula were most common in the region of the duodenum, while alimentary duplications are found most frequently in the lower jejunum and ileum. Nevertheless, it is possible that some duplications have their origins in such diverticula.

According to Keith[7] the development of an alimentary duplication is analogous to that of an atresia. In the latter there is a failure of coalescence of vacuoles in the solid stage of the alimentary tube in its longitudinal axis so that the continuity of the lumen is not established aborally. Keith feels that a duplication results from failure of coalescence of such vacuoles in a transverse manner. Thus, a cystic structure is left contiguous to some portion of the alimentary tract. Bremer[8] supports this theory and points out that the various forms of a duplication's attachment can be explained by the relative distance of the sequestrated vacuoles from the true lumen of the primitive alimentary tube. That is to say, if the sequestrated vacuoles are close to the lumen, the duplication which develops may be separated from the alimentary lumen only by two layers of mucosa, which may undergo necrosis, thus giving a lumenal connection between gut and duplication or, if the distance be greater, submucosal and muscular layers may intervene, until with the greatest degree of separation there may be no attachment at all between the duplication and the alimentary tube.

The ideas of Keith and Bremer offer the most rational explanation of the embryologic development and subsequent form of alimentary duplications as encountered by the surgeon.

CLINICAL ASPECTS

Duplications of the esophagus, like the other forms of alimentary duplication, are usually encountered in infancy and early childhood. Our youngest patient was 3 weeks of age, while the oldest was 22 months. The oldest recorded case in the literature was a boy 3½ years of age.[9] Both sexes are equally involved regarding incidence.

The symptoms caused by esophageal duplication are not only those of an expanding mediastinal mass, but in addition there may be the complicating features of peptic ulceration of the wall of the cyst.

Cough, dyspnea, cyanosis, and recurrent or chronic pneumonias are common presenting complaints referable to pulmonary compression and extrinsic bronchial obstruction by the encroachment of the duplication.

Dysphagia and regurgitation of feedings occur with impingement upon the esophageal lumen.

Apparently pain may be caused by distention of the walls of the duplication with increased intracystic pressure.

Hematemesis and hemoptysis may occur separately or even in the same patient. The former probably results from damage to the blood supply of the esophageal wall by the expansion of the adjacent cyst with resultant sloughing of the esophageal mucosa. Hemoptysis occurred in one individual reported in the German literature[4] as a result of peptic ulcer in an esophageal duplication penetrating into the overlying lung. Three of our patients had repeated hemoptyses as a result of pulmonary compression with superimposed pneumonia.

Physical examination usually discloses definite indications of thoracic disease, but rarely allows the clinician to make a specific diagnosis. Obvious respiratory difficulty and cyanosis are common. Malnutrition and the hallmarks of chronic illness are frequently present. There may be a massive pleural effusion. Signs of chronic pneumonitis and pulmonary compression may be found. Occasionally the duplications are large enough to cause shift of the heart and mediastinum.

Our youngest patient (P. H.), aged 3 weeks, had no apparent symptoms and practically no physical signs of esophageal duplication, the presence of the cyst being disclosed inadvertently by a roentgenogram of the spine taken in the routine orthopedic work-up for club feet.

ROENTGENOLOGIC FINDINGS

Esophageal duplications present roentgen changes characteristic of posterior mediastinal tumors or cysts. Details of the duplication's outline may be obscured by secondary changes in the lung and particularly by pleural fluid. Most duplications are roughly spherical in contour and have a uniform homogeneous density due to their fluid content. The heart and mediastinal structures may be displaced.

Lipiodol bronchograms usually show pulmonary compression by the retropleural duplication, and aid in differentiating the latter from bronchogenic cysts and anomalies. Fluoroscopy of the esophagus with contrast media showed no fistulous connection between duplication and esophagus in any of our patients. However, the esophagus was frequently displaced or angulated by the adjacent mass.

Esophageal duplications occasionally erode the bodies of the thoracic vertebrae or the overlying ribs.

TREATMENT

The most significant fact to be considered in the surgical extirpation of esophageal duplications is that, with rare exception, they share a common muscularis with the esophagus itself. Thus, there is obviously no plane of cleavage to be found between the duplication and the esophagus, and an attempted excision may result in an extensive defect in the esophageal wall. The cyst's attachment is frequently widely sessile. In one of our cases (D. S.) the attachment consisted of about two-thirds of the length of the esophagus.

Because of the nature of the attachment of esophageal duplications, extirpation of the cyst by means of marsupialization with subsequent destruction of the mucosal lining appears to us to be the most conservative and by far the safest procedure. Experience with our own cases seems to bear this out.

In every case we have approached the duplication through a posterior or posterolateral thoracotomy entering the pleural cavity on the side in which the greater portion of the cyst presented. The duplication can usually be readily dissected free from the adjacent lung.

In three instances the duplication was then marsupialized by freeing it thoroughly except from its esophageal attachment and then drawing the most readily available portion into the thoracotomy wound. The pleura was then sutured circumferentially to the wall of the duplication and the chest wall closed in layers, the lung being re-expanded by catheter-suction technique. After the closure of the wound the marsupialized segment of cyst was opened, contents aspirated, and the cavity packed with rough gauze to destroy the mucosal lining (Fig. 7).

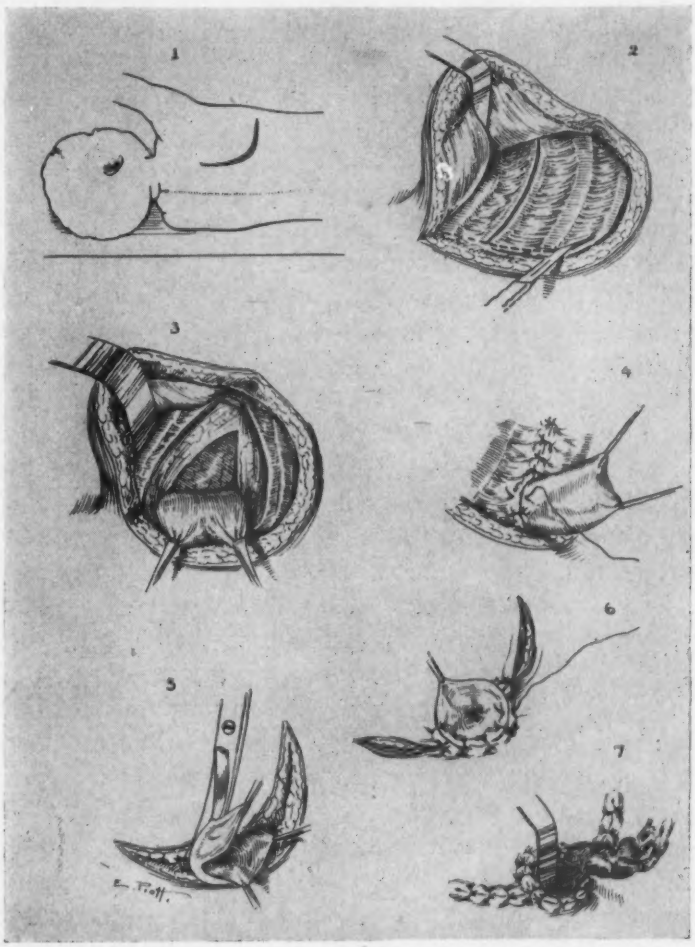


Fig. 7.—Operative drawings showing stages in operative technique of marsupialization of duplication of esophagus.

By adopting this technique the dangerous complications of esophagopleural fistula and mediastinitis are obviated. The mucosal lining of the cyst can be destroyed by packing or by the use of sclerosing solutions, allowing the denuded walls of the cyst to fall together with subsequent spontaneous obliteration of the duplication.

In two individuals an attempt was made to excise completely the marsupialized duplication as a second stage procedure. In one of

these, partial excision of the cyst was done, leaving the medial wall attached to the esophagus and packing this and the pleural cavity with rough gauze. A chronic draining sinus developed, but the esophagus was not damaged and the patient recovered, the sinus closing completely in several weeks. In the other patient, excision of the duplication left a sizable defect in the esophageal wall. Although this was sutured in a seemingly satisfactory manner, a leak developed and an esophagopleural fistula was established. This persisted despite two subsequent attempts at closure and the patient finally succumbed to mediastinal, pleural, and pulmonary infection.

Our fourth patient was treated in a more satisfactory and safer manner by continually packing and curetting the cavity of the marsupialized cyst until the mucosa was destroyed and spontaneous closure of the sinus took place.

In our most recent case (E. B., Case 5) we were unable to make a conclusive diagnosis until almost twelve months after the child's initial hospital entry. The vascular inflammatory tissue which bled so profusely when the mediastinum was entered at the first operation apparently represented the bed of a penetrating peptic ulcer of an esophageal duplication, and because of the profuse hemorrhage and extensive inflammatory reaction the nature of the underlying lesion did not become clear until months later when the persistent wound sinus began discharging "gastric juice." Since we had unwittingly performed a marsupialization, although hardly in a manner to be recommended, it remained a simple matter to excise the sinus, widely exenterating the cystic cavity, and begin destruction of its mucosa by curettage and packing.

The first patient in this group of five cases had a small duplication which could not be found at exploratory thoracotomy, and subsequently he died with pneumonia. At post-mortem examination the duplication was found to be completely free from attachment to the esophagus, and represented one of the extremely rare types which might have been safely excised.

Thus, two of our five patients have died, while the other three have recovered. Follow-up on one of these (D. S.) has continued for sixteen years, another (P. H.) for two and one-half years, and the third (E. B.) is now in good health with the wound healed two months after his last operation. The first two children have developed normally and neither has any demonstrable disturbance of mediastinal or pulmonary anatomy or physiology at the time of this communication. The esophageal duplication has apparently been obliterated in the last individual, but full activity will not be allowed for several months because of the old osteomyelitis.

SUMMARY

1. Duplications of the esophagus are mediastinal cysts of developmental origin occurring along the course of the esophagus.

2. They possess muscular walls and mucous membrane linings which usually simulate gastric mucosa and are subject to peptic ulceration.

3. The cysts frequently have a common wall with the esophagus, thus rendering their complete excision almost impossible without esophageal damage.

4. Five individuals with esophageal duplications have been treated at The Children's Hospital during the last fifteen years. Case histories of these patients are reported in detail.

5. Experience with these individuals indicates that surgical extirpation of a duplication of the esophagus may best be accomplished by marsupialization of the cyst and subsequent destruction of its mucosal lining.

6. Three of our five patients have recovered.

REFERENCES

1. Ladd, W. E.: Duplications of the Alimentary Tract, South. M. J. **30**: 363, 1937.
2. Ladd, W. E., and Gross, R. E.: Surgical Treatment of Duplications of the Alimentary Tract, Surg., Gynec. & Obst. **70**: 295, 1940.
3. Mixter, C. G., and Clifford, S. H.: Congenital Mediastinal Cysts of Gastrogenic and Bronchogenic Origin, Ann. Surg. **90**: 714, 1929.
4. Seydl, Gunther N.: Ein Kongenitale Magenwandcyste in Mediastinalraum mit in die Lunge perforierten Ulcus Pepticum. Frankfurt. Ztschr. f. Path. **52**: 346, 1938.
5. Poncher, H. G., and Milles, G.: Cysts and Diverticula of Intestinal Origin, Am. J. Dis. Child. **45**: 1064, 1933.
6. Lewis, F. T., and Thyng, F. W.: The Regular Occurrence of Intestinal Diverticula in the Embryos of the Pig, Rabbit and Man, Am. J. Anat. **7**: 505, 1907.
7. Keith, Sir Arthur: Human Embryology and Morphology, Baltimore, Md., 1933, William Wood & Company.
8. Bremer, J. L.: Personal communication.
9. von Wyss, H.: Zur Kenntnis des heterologen Flimmercysten, Virchows Arch. f. path. Anat. **51**: 143, 1870.

PRIMARY LYMPHOSARCOMA OF THE BREAST

FRANK E. ADAIR, M.D., AND JULIAN B. HERRMANN, M.D.
NEW YORK, N. Y.
(From the Breast Department of the Memorial Hospital for Cancer and Allied Diseases)

SINCE lymphosarcoma is a disease of the lymphatic structures, any part of the body containing lymphoid tissue may become involved. Enlargement of the superficial, retroperitoneal, or mediastinal lymph nodes is usually the earliest manifestation of the disease process. Later the malady may involve other organs and structures. In some instances the disease process may have its inception in an organ.

An organ infrequently affected by this disease, judging by the paucity of reported cases, is the breast. Gross, in 1880, removed a growth of three months' duration from the upper, outer border of the left mamma of a 22-year-old woman. The histologic diagnosis was lymphadenoid sarcoma. In 1913 Baumgartner wrote, "We know of only two cases of lymphosarcoma of the mamma. The first is that of Billroth and the second is that of Halsam." Geist and Wilensky, in 1915, reviewed the literature on sarcoma of the breast and compiled a list of 435 cases, of which 5 were classified as lymphosarcoma.

The number of authentic examples of breast involvement reported in the literature is further decreased if those are eliminated which are erroneously diagnosed as lymphosarcoma. As an illustration there is the case reported by McWilliams as bilateral lymphosarcoma of the breast in which the biopsy was "benign lymphoma" and the blood picture revealed a leucemia. It may reasonably be assumed that the breast lesions were leucemic rather than lymphosarcomatous manifestations. Also the differentiation between lymphosarcoma and round-cell sarcoma is not always clear. Thus Geist and Wilensky, in their previously mentioned review of breast sarcoma, said, "In two of our cases a previous diagnosis of lymphosarcoma of the breast had been made. The gross and histologic pictures of these tumors correspond accurately with those of round-cell sarcoma." On the other hand, Duany considered as primary lymphosarcoma the case which Heineke reported as round-cell sarcoma of the breast. In Elsberg's case of multiple lymphosarcoma of the breasts, the terms lymphosarcoma and round-cell sarcoma appear to be used interchangeably.

The confusion arises because of the inadequate classification of breast sarcomas. This is emphasized by Ewing, who says, "When one excludes from the group of mammary sarcomas the adenosarcomas, the malignant forms of mixed tumors containing cartilage, bone, mucoid, or fat tissue, and certain malignant round-, spindle-, and giant-cell

Received for publication, May 15, 1944.

alveolar pseudosarcomas, which are really atypical carcinomas, there is little remaining of a once formidable group of mammary neoplasms. There are reasons for believing that such a disintegration of the group is justifiable. In fact, the situation today is much as it was in 1894, when Williams found it impossible to write the history of pure mammary sarcoma because of the absence of requisite data.

The round-cell sarcomas of various authors form an ill-defined group. They probably include very atypical tumors of the same nature as unclassified spindle-cell sarcomas, atypical carcinomas, and some pigment-free melanomas."

Lymphosarcoma of the breast may be a local manifestation of the disease which has originated elsewhere in the body, or it may be a primary lesion in this organ. The secondary focus may be a discrete metastatic lesion or it may be a direct extension from a mediastinal tumor. An example of the latter mode of involvement of the breast is the case described by Schoen. The patient had suffered from gynecomastia in his youth. This subsided, but at the age of 38 years both breasts underwent painless enlargement with no other evidence of disease. Eight months later nodules appeared in the skin of the scalp and trunk, followed by cervical and axillary lymphadenopathy. The patient died six months later and an autopsy revealed generalized lymphosarcomatosis with a huge mediastinal tumor and massive involvement of both breasts. There was a direct connection between the mediastinal tumor and the tumor in the left breast through the intercostal muscles. The tumor in the right breast was unconnected with the mediastinal mass.

Various writers on the subject of lymphosarcoma of the breast have been at a loss to explain the occurrence of the disease in this organ. Geist wrote, "We were unable to demonstrate that lymphoid tissue occurred normally either in the breast proper or in the skin overlying it, nor could we find references in the literature to its occurrence, and we were forced to conclude that lymphosarcoma does not occur primarily in the breast and that the tumors so classified heretofore were in all probability small, round-cell sarcomata." In his paper on lymphosarcoma of the breast Harrington says, "The explanation for the presence of a primary lymphosarcoma of the breast is rather difficult, since lymph follicles are not ordinarily located there, but the following suggestions may be made. Large collections of lymphocytes are found in the mammary gland in most chronic pathologic entities affecting the breast. Secondary lymph follicles may be formed and a continuation of the stimulus, whatever it is, may produce a malignant change."

On this phase of the subject Stewart and Foote* were kind enough to contribute the following explanation: "There are commonly found

*Dr. Fred Stewart and Dr. Frank Foote of the Department of Pathology, Memorial Hospital.

in the breast lymphoid infiltrates in the lobules and about the ducts. These, sometimes, are highly developed and contain definite germinal centers. There is every reason to believe that these are the origin of the lymphomas. Moreover, in some of the cases of lymphosarcoma seen at this hospital there are found foci of lymphomatous infiltrates of benign appearance and not in direct continuity with the true lymphosarcoma."

There are some intra- and juxta-node groups which may possibly be the site of origin of the disease in some instances. Their location may be indicated most clearly by the following brief description of the breast lymphatics (Fig. 1).

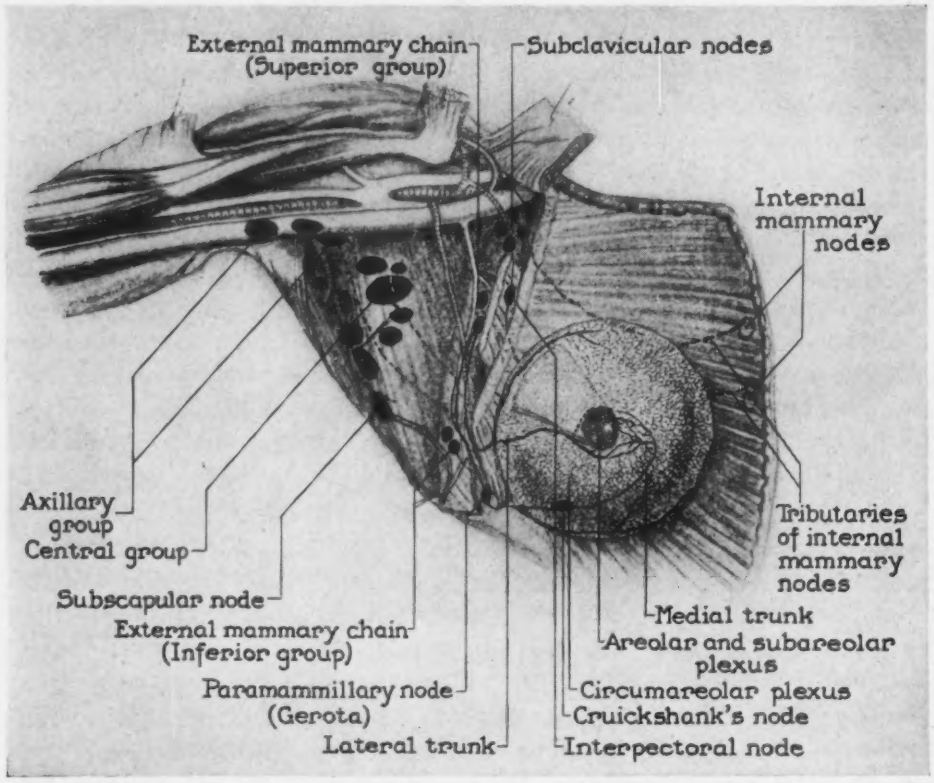


Fig. 1.—Lymphatics of the breast. (Adapted from Rouviére, Anatomy of the Human Lymphatic System. Translated by Tobias, Ann Arbor, 1938, Edwards Brothers, Inc.)

As in other regions of the body, the lymphatic system of the breast is composed of two elements: vessels and nodes. The cutaneous lymphatic vessels form a dense network lying in several planes in the areolar region. The most superficial of the areolar plexus is continuous with the lymphatics of the skin of the breast. Beneath this superficial plexus and connected with it is the subareolar plexus. This plexus receives the major portion of the lymphatics of the mammary gland.

The meshwork of lymphatics which is dense in the subareolar region thins out toward the periphery of the gland and in this location is

known as the circumareolar plexus. This plexus at its outer aspect is continuous with and has the same configuration as the lymphatics of the anterior thoracic wall.

The lymphatic trunks of the mammary gland proper arise in the inter- or perilobular network. Some of these vessels then follow the lactiferous ducts, receive lymphatics from them, and finally terminate in the subareolar plexus. Other lymphatic trunks do not enter the subareolar plexus but traverse the gland to its periphery where they emerge to terminate in the axillary nodes. Still other trunks run posteriorly with the perforating vessels to terminate in the internal mammary chain of nodes. Occasionally a trunk terminates directly in the transverse cervical chain of nodes.

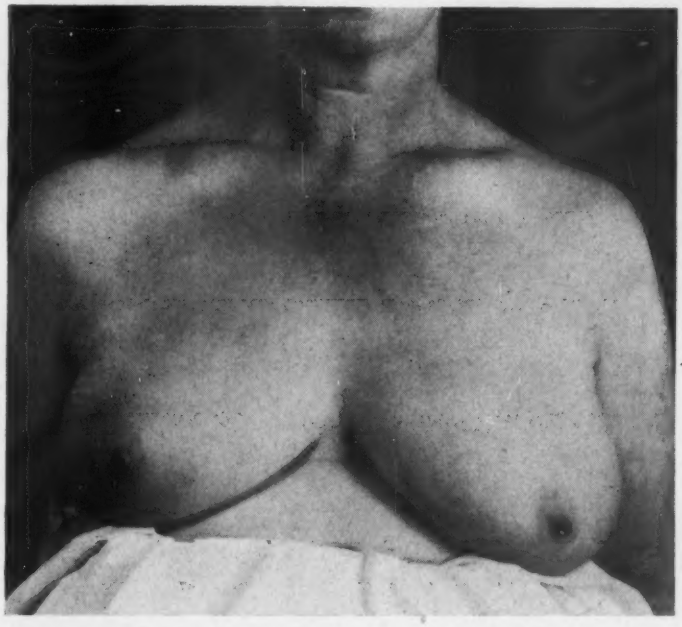


Fig. 2 (Case 1).—Elevation of right breast and retraction of the nipple are well marked. The deformity produced by the tumor is visible on the 11 o'clock radius.

Two large collecting trunks, a medial and a lateral, connect the subareolar network with the axillary nodes, the former draining the upper aspect of the breast and the latter the lower part.

Lymph nodes are found in association with the lymphatic vessels and may be divided into three groups:

First, the small cutaneous nodes described by Cruikshank. These lie between the integument and the exterior surface of the mamma and are situated between the nipple and the axilla, in association with the collecting lymphatic trunks running to the axillary nodes.

Second, the nodes described by Kermisson. These are few in number but are consistently present, lying deep in the gland in association with the lymphatic trunks that follow the lactiferous ducts. To quote

Kermisson's description, "They are so intimately connected with the gland structures that at times it is difficult to decide whether a tumor is composed of mammary tissue itself or if it is formed from these nodes."

Third, the paramammary nodes described by Gerota which are not in the strict sense of the word mammary nodes. They do not lie in the gland but are situated just outside of it in the anterior abdominal wall.

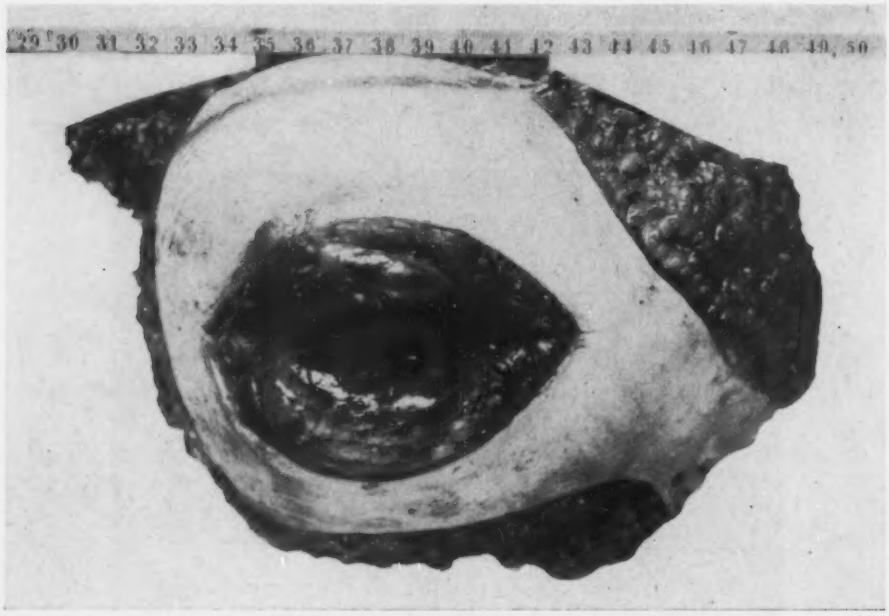


Fig. 3 (Case 1).—The tumor lies in the fat just below the skin and is well circumscribed.

Description of Gross Specimen: A fat breast with residue of thickened ducts. Prominently bulging the breast just below and external to the nipple was a large, freely movable, fairly soft, elastic, rubbery, circumscribed tumor measuring 6 by 5 by 5 cm. On section the tumor was soft, pinkish gray with areas of hemorrhage. In the axilla were several enlarged nodes which, however, consisted of a thick periphery of lymphoid tissue surrounding bulky fat lobules.

Since the breast commonly contains lymphoid infiltrates and some lymph nodes, the possibility of involvement of this organ by lymphosarcoma is readily explained. Secondary involvement by the disease is probably more common than a study of the literature would indicate. The breast is not usually sectioned routinely at autopsy so that localized disease in this organ, too small to give physical signs, may be easily overlooked.

Primary lymphosarcoma of the breast is an uncommon disease. In true primary lymphosarcoma of the mamma the disease arises here and remains localized a longer or shorter period of time. In order to establish this diagnosis there must be no evidence of the disease outside the breast. This is self-evident since the etiology of the disease and its mode of spread is unknown, although Willis believes it extends predominantly by lymphatic routes, spreading from node to node. Hence if two foci are

present at the initial examination (for example, a mass in the breast and enlarged ipsolateral axillary nodes), it cannot be determined which is the primary lesion. Similarly if a nodule is present in both breasts one may be primary and the other metastatic, unless the theory that the disease may be multicentric in origin is adopted.

The definition and classification of the manifestations of breast lymphosarcoma are important from the standpoint of treatment and prognosis. The following classification is proposed.

1. Primary lymphosarcoma of breast
   - A. Localized unilateral
     - (a) Single focus
     - (b) Multiple foci
   - B. Diffuse bilateral
2. Secondary lymphosarcoma of breast

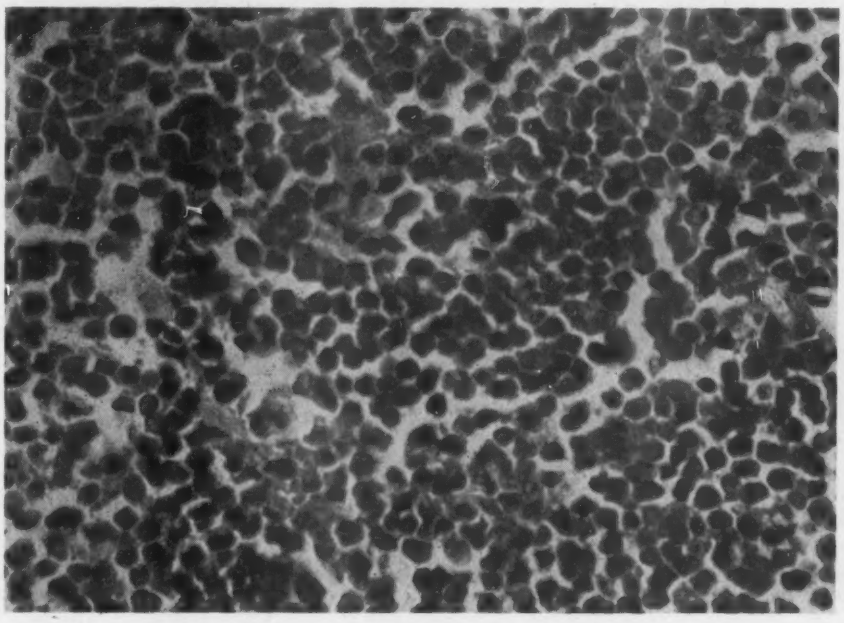


Fig. 4 (Case 1).—Reticulum-cell lymphosarcoma (×225).

The diffuse type is an interesting condition. Cases have been reported by many clinicians (Pasqualino, Dellepiane, Billroth, Frascella). The majority of them occurred in young, pregnant Italian women, either nulliparas or multiparas, in their late twenties and early thirties. The condition, which is bilateral, manifests itself during the early months of pregnancy when the breasts enlarge quickly and soon reach a huge size. The enlargement may start simultaneously in both breasts or it may begin in one before the other.

Examination reveals huge, pendulous breasts in which the skin may be infiltrated, of a pinkish or violaceous hue, enlarged veins, and elevated surface temperature. The appearance is often similar to that

seen in carcinomatous skin infiltration. On palpation there is no tenderness but the mammae are hard and indurated. The axillary lymph nodes soon enlarge. The mammary glands, in the reported cases, weigh from 5 to 10 pounds each. Blood studies reveal nothing of importance except an occasional secondary anemia.

The disease is rapidly progressive, the outstanding symptoms being anorexia and weight loss. The patient usually goes through the pregnancy, is delivered of a normal baby, and dies within a few months after parturition. These breasts do not lactate. Autopsy reveals a disseminated lymphosarcomatosis.

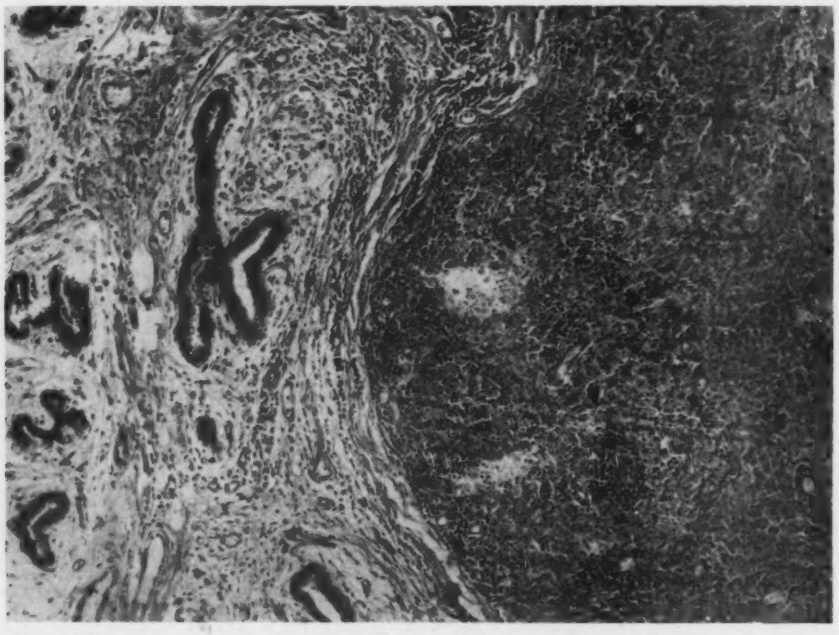


Fig. 5 (Case 2).—The tumor is well circumscribed and does not invade the breast tissue (×45).

Description of Gross Specimen: A radical mastectomy with skin ellipse measuring 26 by 11 cm. Near the center of the ellipse was a retracted nonulcerated nipple. When the breast was sectioned, in the lower portion of the upper outer quadrant a tumor nodule measuring approximately 2.5 cm. in diameter was found. It was lying approximately 4 cm. from the inner line of transection of the specimen and also was lying 3 cm. deep to the skin and approximately the same distance above the pectoral muscles. The bulk of the tumor on cross section was composed of soft, yellow-gray necrotic tissue. However, there was a rim of translucent gray, nodular, firm tumor tissue apparently still viable. The remainder of the breast tissue was firm and fibrous where it was not replaced by fat and no lobulations could be seen grossly. The ducts were not dilated but were surrounded by increased amounts of connective tissue. No grossly involved nodes were found in the axilla.

Ewing has raised the question, specifically in connection with the case described by Billroth, whether this condition is a variety of rapidly growing atypical carcinoma of pregnancy. The consensus of opinion, however, of those who have had an opportunity to study this disease is that it is lymphosarcoma.

There is a similar type of diffuse involvement of the breast seen in Hodgkin's disease.* This, however, may be unilateral and is secondary to a generalized process.

*To be published.

Localized lymphosarcoma of the breast is a rare condition. During the past twenty years 4,445 patients with benign tumor and 6,519 patients with malignant tumor were seen on the breast service of the Memorial Hospital. Of this total of 10,964 patients, only five had primary localized lymphosarcomas. One of these patients underwent a local excision of the tumor at another institution prior to admission to the Memorial Hospital clinic. The pertinent data of the five cases have been tabulated (Table I). A review of the literature discloses but two additional cases, that of Harrington and that of Fox, which satisfy the criteria for primary lymphosarcoma of the breast.

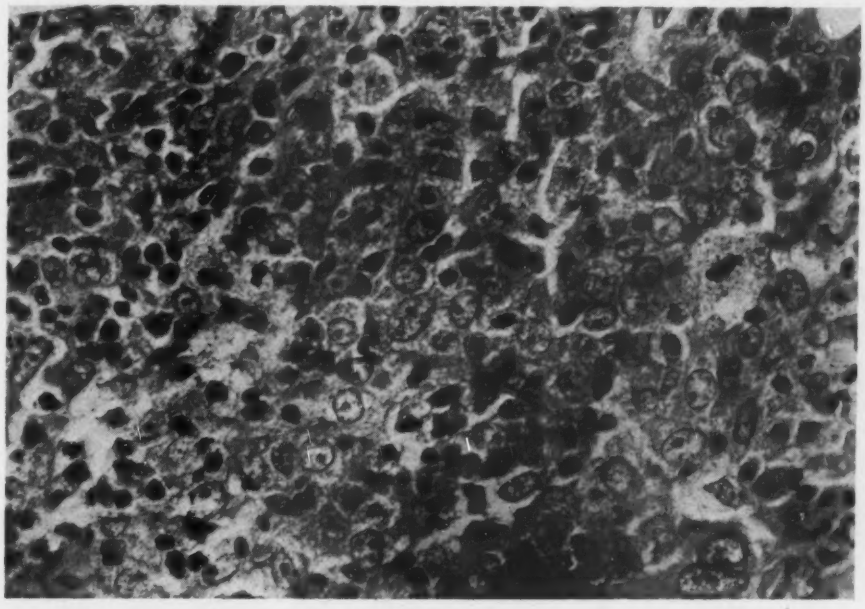


Fig. 6 (Case 2).—Higher magnification of the reticulum-cell lymphosarcoma shown in Fig. 5.—(×225).

Our series is much too small to permit of accurate conclusions. However, a few generalities will be attempted. The patients were white women in the fourth or fifth decade. Their average age was 50 years, 3 months. The elapsed time between the discovery of the tumor and the institution of therapy was short; from two to four weeks. The right breast was involved in four of the five patients. With the exception of one patient in whom the affected breast contained two lesions, the involvement occurred as a single focus of disease. The lesion was located in the upper outer aspect of the right breast in four of the patients. The mass in every instance was small, ranging in diameter from 1 cm. (the smallest) to 4 cm. (the largest). Of the four patients seen before operation there was nipple retraction in one and skin attachment or dimpling in three. X-ray studies of the chest were made in three patients and revealed an absence of pulmonary or medi-

TABLE I

CASE	(YR.) AGE	INITIAL SYMPTOM	DESCRIPTION OF BREAST	PAST HISTORY	PROVISIONAL DIAGNOSIS	ASPIRATION BIOPSY	GENERAL EXAMINATION	BLOOD	URINE	TREATMENT	PATHOLOGIC EXAMINATION	PROGRESS
1	53	Discovered painless mass in right breast two weeks before admission to hospital; some increase in size	Right breast, 4 cm. mass with skin attachment on radius of 11 o'clock near nipple; nipple retracted; no discharge	Gravida 1; para I; menopause 2 yr. previously; nursed with left breast—never with right	Malignant tumor	Lymphomatous process	No lymphadenopathy or other evidence of disease; x-ray of chest negative	Hb., 75% R.B.C., 3.8 W.B.C., 13,600 Polys., 74 Large lymph., 4 Small lymph., 18 Trans., 3	Acid Albumin 0 Sugar 0 Many pus and R.B.C.	Radical mastectomy	Reticulum-cell lymphosarcoma; nodes showed hyperplastic germinal centers but nothing which could be called lymphosarcoma	No evidence of disease 7 yr. after operation
2	47	Discovered painless lump in left breast 1 week before admission to hospital; no increase in size; some pain in left chest radiating posteriorly	Left breast, 2 cm. mass, slightly tender on 11 o'clock radius 4 cm. beyond areola; suggestion of skin dimpling could be produced over it; left nipple slightly elevated, not stuck; no discharge	Menstrual 13 × 28 × 4-5; sister had carcinoma of breast	Cyst	Carcinoma, probably large cell medullary type with much lymphocytic infiltration	No lymphadenopathy or other evidence of disease; x-ray of chest negative	Not examined	Acid Albumin 0 Sugar 0 Occasional leucocytes	Radical mastectomy	Appeared to be primary mammary reticulum-cell sarcoma; nodes clear	No evidence of disease 3 yr. after operation

3	41	Fell and bruised right breast 4 mo. previously; 2 mo. later noticed painless lump in the area which had been discolored; 1 mo. later lump excised at another hospital; diagnosis of lymphosarcoma made and patient referred to this institution for further treatment	Curved scar 3 cm. long, somewhat indurated, in right breast on radius of 8 o'clock just beyond areola	Gravida 4; para IV; nursed 3 infants; caking of breasts during lactation; menstrual 17 × 28 × 3-4			No other evidence of disease; x-ray of chest negative; subsequently developed slight yellowish discharge from left nipple which was diagnosed as duct stasis	Hb., 85% R.B.C., 4.3 W.B.C., 8,900 Segmented, 59 Lymph., 36 Monos., 3 Eos., 1 Mast cells, 1	Not examined	Radiation right breast laterally; 250 Kv., T.S.D. 50, field 8.5 × 25 cm., 30 M.A., 300 r. × 8, total 2400 r.	Submitted slide; consistent with lymphosarcoma	No evidence of disease 1½ yr. after operation
4	53	Discovered painless mass in upper outer quadrant right breast 2 weeks previous to admission to hospital	Right breast in upper outer quadrant, firm tumor 2.5 cm. in diameter with skin attachment and dimpling over it; superficial veins enlarged; no nipple retraction or palpable nodes	Gravida 1; para I	Carcinoma	Malignant tumor; not sure whether lymphosarcoma or carcinoma; former favored	No other evidence of disease; no chest x-ray taken	Not examined	Albumin 0 Sugar 0	Radical mastectomy	Reticulum-cell sarcoma; nodes negative	No evidence of disease 3 mo. after operation

TABLE I—CONT'D

CASE	AGE (YR.)	INITIAL SYMPTOM	DESCRIPTION OF BREAST	PAST HISTORY	PROVISIONAL DIAGNOSIS	ASPIRATION BIOPSY	GENERAL EXAMINATION	BLOOD	URINE	TREATMENT	PATHOLOGIC EXAMINATION	PROGRESS
5	58	Painless lump in right breast for 3 weeks	Right breast, 2 firm, freely movable masses 1 cm. in diameter; 1 on the radius of 7 o'clock and other on that of 9 o'clock	Hysterectomy 13 yr. previously followed by artificial menopause	Fibroadenoma	Lymphoid tissue; in this location lymphosarcoma could not be excluded	1 cm. node in right axilla; no chest x-ray taken	Hb., 75% R.B.C., 3.7 W.B.C., 8,400 No differential	Albumin 0 Sugar 0	Local excision followed immediately by simple mastectomy and low axillary dissection	Follicular lymphosarcoma (follicular and diffuse Brill-Symmers disease); there are lymphoid aggregates in the breast, although not in association with true breast tissue, and also in the axillary nodes	No evidence of disease 6 mo. after operation

astinal involvement. Blood studies, in the cases when they were carried out, gave normal findings.

All of the patients, with the exception of the one who underwent a local excision of the tumor at another clinic, were treated exclusively by surgery. The procedure in three was a radical mastectomy and in the fourth a simple mastectomy with a low axillary dissection. The patient whose tumor had been locally excised previous to consultation at this clinic was treated with high voltage x-ray applied to the area of excision. The axilla was not radiated.

The pathologic report was reticulum-cell sarcoma in three of the patients operated on and follicular lymphosarcoma (Brill-Symmers' disease) in the fourth. The slide submitted from the case in which the tumor was excised at another clinic was interpreted as "consistent with lymphosarcoma." No axillary node involvement was found in any patient. In two of the patients (Cases 4 and 5) the pathologist's description of the gross findings was very suggestive that the process had its inception in the nodes described by Cruikshank. The description of these gross specimens is given with the respective photomicrographs (Figs. 8 to 11). All the pathologic studies were made by Dr. Fred Stewart and his associates.

The protean nature of the lesion may be judged from the provisional diagnoses which were carcinoma, malignant lesion, cyst, and fibroadenoma. The various conditions which must be considered in a differential diagnosis and the diagnostic criteria are given in Table II. The only points suggestive of diagnostic significance are that the mass occurred in the upper outer quadrant of the right breast in four of our five patients, and that the mass in every instance was small, less than

TABLE II

DIFFERENTIAL DIAGNOSIS OF BREAST NODULES

DISEASE	PRESUMPTIVE EVIDENCE	CONCLUSIVE EVIDENCE
Carcinoma	Skin attachment; nipple retraction	Biopsy
Cyst	Transillumination; fluctuation	Aspiration
Leucemia	Generalized lymphadenopathy	Blood picture
Primary lymphosarcoma	Small mass in upper outer quadrant; 4th or 5th decade of life	Biopsy
Secondary lymphosarcoma	Generalized lymphadenopathy	Biopsy
Hodgkin's disease	Generalized lymphadenopathy	Biopsy
Sarcoma	Rapidly growing; large size	Biopsy
Chloroma	Generalized lymphadenopathy; osseous changes	Green color on section
Tuberculosis	Pulmonary tuberculosis; sinus tract	Biopsy

4 cm. in diameter. The latter finding may be due to the fact that the lesions were discovered early. These criteria are of little differential diagnostic value since carcinoma occurs frequently in that location, in the same age group, and with the same characteristics. That the condition may closely simulate carcinoma is exemplified by the circumstance that this was the provisional diagnosis in two of the patients in the present series. In cases reported by Ghon and Roman and by Clairmont, the patients underwent a radical mastectomy for supposed carcinoma of the breast which subsequently was proved to be lymphosarcoma. A post-mortem examination revealed a large mediastinal tumor as part of a widespread abdominal lymphosarcomatosis.

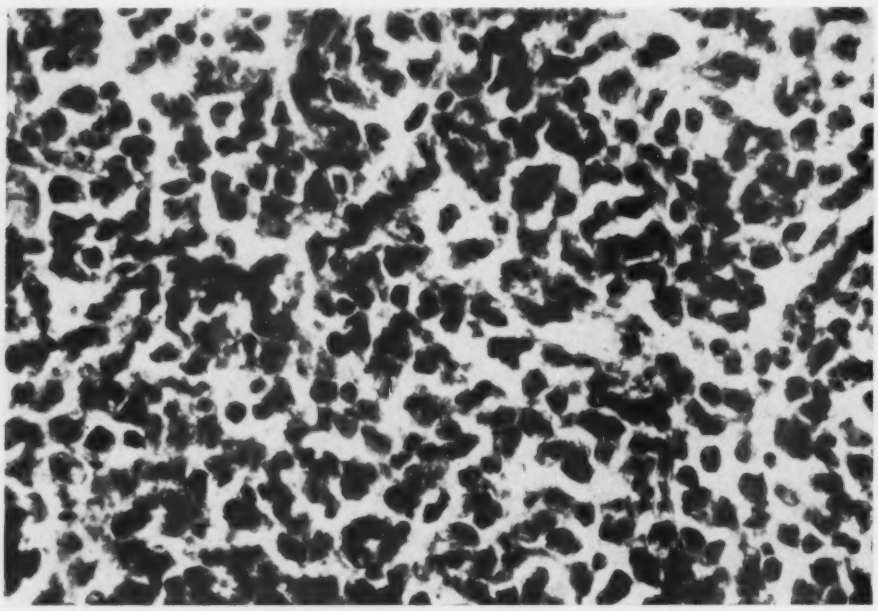


Fig. 7 (Case 3).—Lymphosarcoma (×225).

This type of error can be avoided by a preoperative chest x-ray. A mediastinal mass is suggestive of lymphoma or metastatic carcinoma, either of which is a contraindication to surgery. The blood examination is also important as a diagnostic aid in breast nodules caused by leucemia or chloroma. In the ultimate analysis the correct diagnosis can be made only when the tumor is removed and examined microscopically, although the aspiration biopsy findings were suggestive of a lymphomatous process in every one of our patients.

Primary lymphosarcoma of the breast, like that of the stomach, is a distinct entity. This form of the disease may be of lower-grade malignancy than generalized lymphosarcoma and may tend to remain localized for a considerable period of time. For that reason early recognition is important since the disease is amenable to surgery in its localized phase. Gall has recently published a series of forty-eight cases of lymphoma of different organs and structures in which the

patients were treated by surgery with an average survival period of 5.2 years. This figure is about double that obtained by other methods of treatment in similar cases.

Three of our patients were treated by radical mastectomy and are alive and free of disease seven years, three years, and six months, respectively. One patient was treated by local excision of the lymphomatous nodule followed by deep x-ray therapy and is alive and free from disease one and one-half years after the surgical procedure. In one patient a simple mastectomy with low axillary dissection was performed. This patient is alive and free from disease three months following operation.

A survey of the reported cases of lymphosarcoma of the breast in which the patients were treated by surgery (Seidemann, Ghon and Roman, Clairmont, Finsterer, Kundrat, D'Aunoy and Wright, Schreiner and Thibaudeau, Fox, Hill and Stout, and Harrington and Miller) re-

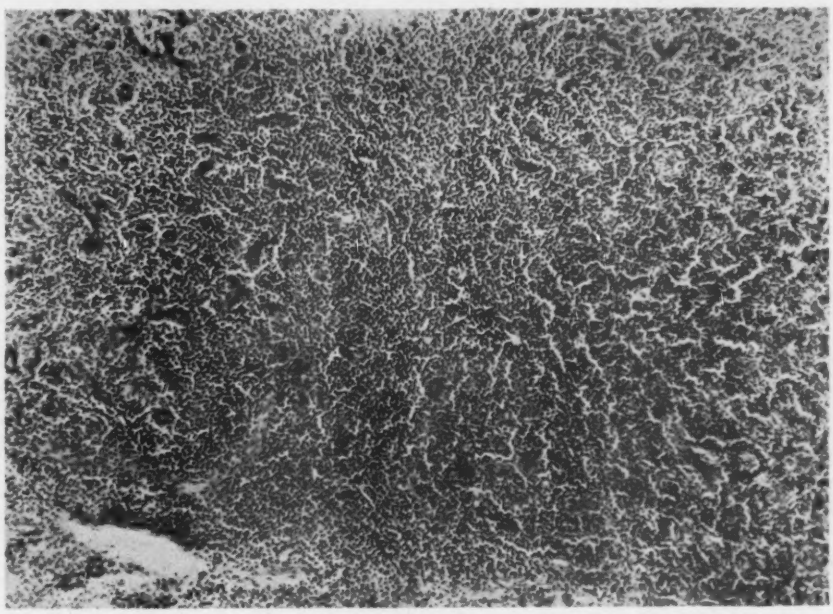


Fig. 8 (Case 4).—Reticulum-cell lymphosarcoma, low magnification (×45).

Description of Gross Specimen: Moderate-sized radical mastectomy of the right side. Five centimeters from the nipple was an area of skin dimpling. Beneath this area of skin alteration a not too well-defined but firm tumor could be felt. On section the central portion of this tumor lay 7 cm. from the base of the nipple. *The tumor lay in the fat and connective tissue which separated the skin from the underlying breast tissue.* On first glance there was a fleeting impression that the tumor was lipomatous but after complete section this false appearance was seen to be due to the fact that the tumor at its periphery merged almost imperceptibly with the lobules of fat. The tumor measured about 5 cm. in its greatest dimension with the bulk of the tumor being about 3.5 cm. It was unencapsulated and not well demarcated, since there were peripheral extensions into and between the fat lobules. After section the tumor did not feel firm but was of the same density as lymphoid tissue. The solid part of the tumor had the fish-fleshlike appearance of lymphoid tissue. The breast tissue showed but little fat replacement. There was moderate dilation of most of the larger mammary ducts and they contained creamy yellowish material. Not a single cyst was seen and no other lesions were grossly visible. The mammary lobules were fairly numerous and seemed rather small. In summary, the breast tissue was unusually homogeneous. Eighteen nodes were dissected from various areas in the axilla. These were pea sized or slightly larger save for one node which was 1.5 cm. in diameter. This node was slightly firm at one point near its capsule but definite structural alteration was not seen.

veals that with the exception of the patient of Harrington and that of Schreiner, none survived more than a few months. Schreiner's patient had palpable nodes in the right axilla at the time the right radical mastectomy was performed. Although she soon developed widespread metastases, these were controlled by irradiation for a period of almost five years, after which there is no record. Harrington's patient was alive and free of disease six years after radical mastectomy. D'Aunoy gives no information relative to his patient's postoperative course, and Hill's patient was followed for only four months. All of the other patients retrogressed rapidly, death apparently being hastened by the operation. An analysis of these cases reveals that, with the exception of one of Harrington's patients and one of Fox's, in no instance do they

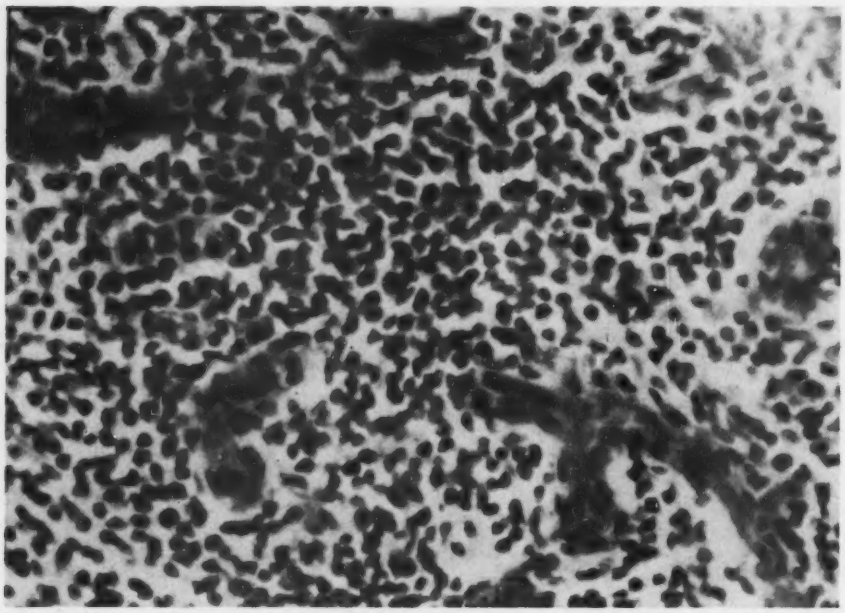


Fig. 9 (Case 4).—Higher magnification of a portion of the field shown in Fig. 8 (×225).

satisfy the foregoing criteria given for primary lymphosarcoma. At the time of the first examination all of these other individuals presented more than local evidence of the disease. In some instances they gave a history of a primary nodule in the breast, but since no examination was made at that time, the history alone was not reliable.

On the basis of the foregoing facts it would seem that lymphosarcoma of the breast should be treated by surgery only if the disease is localized in the breast and confined to one breast. Impressed by the gratifying results from surgery of primary localized lymphosarcoma in other parts of the body, notably the gastrointestinal tract, we believe this mode of therapy to be effective. Our patient who lived

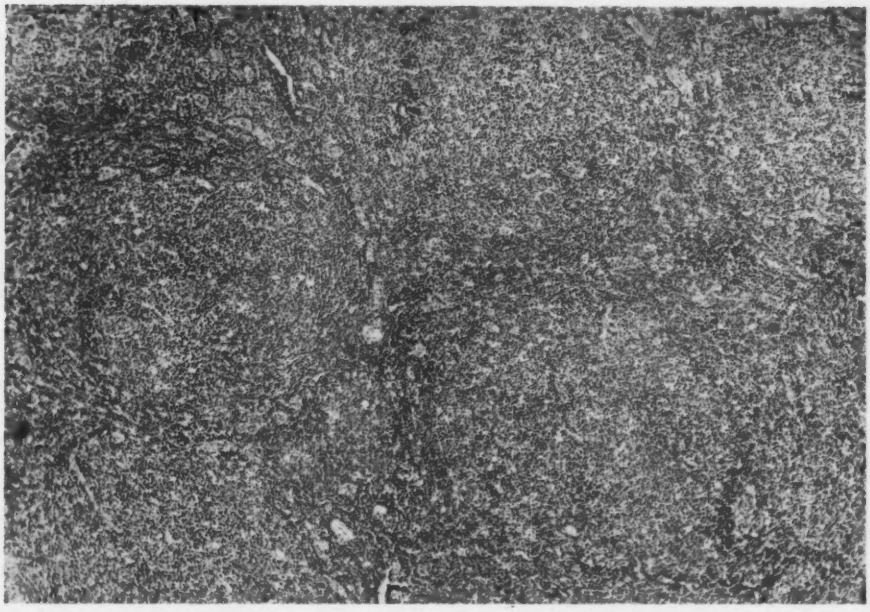


Fig. 10 (Case 5).—Follicular lymphosarcoma (×45).—Three contiguous follicles are shown.

Description of Gross Specimen: The locally excised breast tissue revealed the presence of two tumor masses each measuring about 1 cm. in diameter, rather soft in consistency. The cut section showed a homogeneous yellowish surface which had the gross appearance of lymphoid tissue. *The nodules were definitely not in the node-bearing area; neither were they in the breast proper but in the subcutaneous fat overlying the breast tissue.*

The breast itself showed nothing of note. Several enlarged nodes were encountered in the axilla at all levels, varying between 8 mm. and 3 cm.

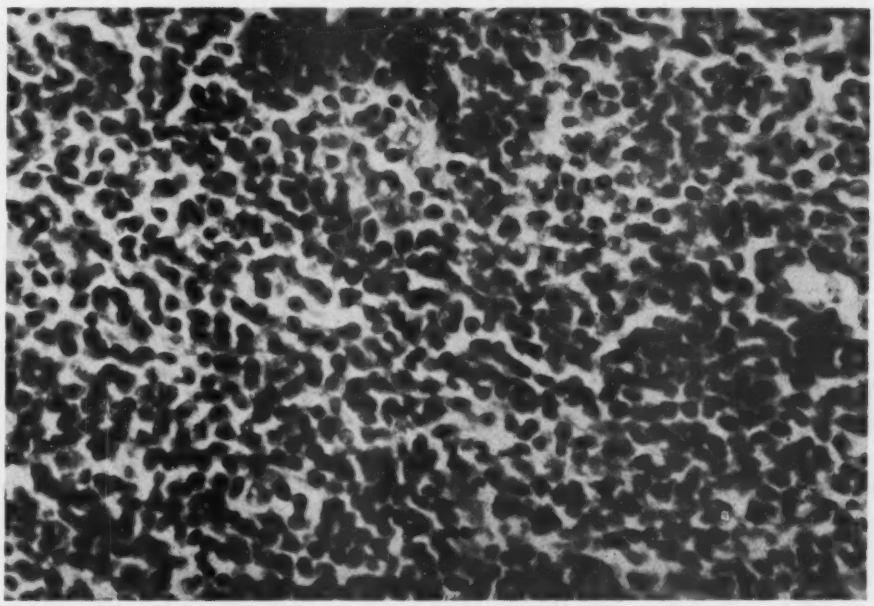


Fig. 11. (Case 5).—Follicular lymphosarcoma (×70). This is a higher magnification of a portion of a follicle shown in Fig. 10.

seven years and that of Harrington tend to support this view. The other cases in our series are too recent to be of value in basing conclusions.

If there is other evidence of disease in addition to that in the breast, then surgery is contraindicated and the patient is best treated as a case of generalized lymphosarcomatosis. Whether the prognosis in the cases of multiple nodules in the same breast is different from that in which the lesion is solitary cannot be determined from this small group. Only one of the patients in the present series had multiple foci in the breast. This patient is free from evidence of disease one-half year after her simple mastectomy.

SUMMARY AND CONCLUSIONS

1. Primary lymphosarcoma of the breast is a rare lesion.
2. A classification of breast lymphosarcoma is proposed.
3. The lymphatic system of the breast and its correlation with lymphosarcoma are described.
4. Five cases of primary breast lymphosarcoma are reported, in which all the patients are alive and free from disease following surgery for periods ranging from seven years to three months.
5. We believe that in primary lymphosarcoma of the breast, as in primary gastrointestinal lymphosarcoma, radical surgery is the procedure of choice.
6. Criteria for operability are set forth.

REFERENCES

1. Baumgartner, A.: Maladie de la Mammelle. Nouvean Traité de Chirgurie, Paris, 1913, Le Dentu et Delbet, p. 323.
2. Billroth, L.: Handbuch der Frauenkrankheiten, vol. 3, Stuttgart, 1877-1880, F. Enke.
3. Clairmont, P.: Einige Fälle von Seltenen Geischwulstmatastasen, Arch. f. klin. Chirg. **89**: 513, 1909.
4. Cruikshank, W.: Anatomy of the Absorbing Vessels of the Human Body, ed. 2, London, 1790, J. Nicol.
5. D'Aunoy, R., and Wright, R.: Sarcoma of the Breast, Ann. Surg. **92**: 1059, 1930.
6. Dellepiane, G.: Linfoblastoma bilaterale della mammella simulante una ipertrofia mammaria gravidica, Riv. ital. di ginec. **11**: 162, 1930.
7. Duany, N. P.: Linfosarcoma de las glandulas mammarias, Bol. Liga contra el cáncer **16**: 65, 1941.
8. Elsberg, C. A.: Multiple Lymphosarcoma of Both Breasts, Ann. Surg. **60**: 767, 1914.
9. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, 1940, W. B. Saunders Co., p. 557.
10. Finsterer, J.: Ueber das Sarkom der weiblichen Brüstdrüse (Case 23), Deutschie Ztschr. f. Chir. **86**: 352, 1907.
11. Fox, S.: Sarcoma of the Breast, Ann. Surg. **100**: 401, 1934.
12. Frascella, P.: Linfoblastomastosi sistemica mammaria simulante una ipertrofia patologica gravidica, Tumori **10**: 343-360, 1924.
13. Gall, E. A.: The Surgical Treatment of Malignant Lymphoma, Ann. Surg. **118**: 1064, 1943.
14. Geist, S., and Wilensky, A.: Sarcoma of the Breast, Ann. Surg. **62**: 11, 1915.
15. Gerota, D.: Cited by Rouviére, H.: Anatomy of the Human Lymphatic System, translated by Tobias, M. J., Ann Arbor, 1938, Edwards Brothers, Inc., p. 129.

16. Ghon, A., and Roman, B.: Ueber das Lymphosarkom (Case No. 8), Frankfurt. Ztschr. f. Path. **19**: 1, 1916.
17. Gross, S. W.: Tumors of the Mammary Gland, New York, 1880, Appleton & Co.
18. Halsam, W.: Birmingh. M. Rev. **25**: 286, 1889.
19. Harrington, S. W., and Miller, J. M.: Lymphosarcoma of the Mammary Gland, Am. J. Surg. **48**: 346, 1940.
20. Heineke, H.: Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlen auf das Knochenmark nebsteinigen Bemerkungen über die Röntgentherapie der Leukämie und Pseudoleukamie und des Sarcoms (Case No. 3), Deutsche Ztschr. f. Chir. **78**: 197, 1905.
21. Hill, R., and Stout, A.: Sarcoma of the Breast, Arch. Surg. **44**: 723, 1942.
22. Kermisson, E.: Bull. de la Soc. Anat. de Paris, 4e Serie **7**: 453, 1882.
23. Kundrat, Prof.: Ueber Lympho-Sarkomatosis, Wien.-klin. Wchnschr. **6**: 211, 1893.
24. McWilliams, C. A.: Bilateral Lymphosarcoma of the Breasts, Ann. Surg. **55**: 439, 1912.
25. Pasqualino, G.: Linfoblastoma bilaterale delle mammelle, Tumori **18**: 172, 1932.
26. Schoen, R.: Lymphosarkomatose mit Beiteiligung der Bruste bei einem Gynäkomasten, Frankfurt. Ztschr. f. Path. **25**: 112, 1921.
27. Schreiner, B., and Thibaudeau, M.: Sarcoma of the Breast, Ann. Surg. **95**: 433, 1932.
28. Seidemann, H.: Seltener Mammatumor, Monatschr. f. Geburtsh. u. Gynäk. **78**: 310, 1928.
29. Willis, R.: The Spread of Tumors in the Human Body, London, 1934, J. & A. Churchill, Ltd., p. 38.

MIXED MALIGNANCY OF THE BREAST

Case Report of a Combined Carcinoma and Sarcoma in a Child, With Review of the Literature

H. G. Smithy, M.D., Charleston, S. C.

(From the Departments of Surgery of The Medical College of the State of South Carolina and Roper Hospital)

THE simultaneous occurrence of two different malignant processes at points of origin quite distinct and separate from each other is a well-established entity. The papers of Wells,[1] Loeb,[2] Major,[3] and others[4-6] indicate that multiple primary malignant tumors are not rare. Much less common than these anatomically unrelated tumors is the presence of two different types of neoplastic tissue growing within the same organ.

Mixed malignancy of the breast can be divided into two categories: (1) the simultaneous presence of two distinct varieties of malignant tumors growing side by side but having no structural intermingling of their elements, and (2) a combination growth of two different malignant tissues whose component parts are intimately blended with one another into a single tumor.

The first type may be regarded as a coincidental occurrence of two independent neoplasms in the same organ. Kettle[7] and Curphey[8] each reported one case of fibrosarcoma and invasive carcinoma of the breast, the malignant elements existing as separate tumors and showing no structural intermingling. In a case recorded by Schwarz,[9] the patient was operated upon for carcinoma of the left breast; three years later she developed a sarcoma in the right breast which also showed metastatic carcinoma from the original tumor, apparently unrelated to the sarcoma. A similar instance was reported by Lester,[10] in which radical mastectomy for cancer was followed in fifteen months by recurrence of the epithelial tumor in the scar, associated with a neurogenic sarcoma. The simultaneous occurrence of these two tumors was regarded as coincidental.

The second type of mixed tumor of the breast can hardly be considered as an accidental coexistence of different neoplastic lesions. Intimate association of both epiblastic and mesoblastic components, homogeneously blending into a single tumor, is probably more than accidental. It appears likely that these tumors either arise from a single cell, or one element occurs first and subsequently stimulates proliferation of the other. Experimentally, the appearance of malignant stroma in a previously pure carcinoma has been demonstrated in

Received for publication, June 15, 1944.

mice. Ehrlich and Apolant,[11] Haaland,[12] and Russell[13] independently established beyond doubt the metaplastic property of mammary connective tissue in which adenocarcinoma is growing. In the tenth generation transplants of breast cancer in mice, Ehrlich and Apolant obtained a malignant tumor which exhibited sarcomatous properties as well as the original epithelial element. Russell's animals showed a similar change in which previously normal connective tissue stroma cells were gradually transformed into malignant sarcoma cells. About fifty-five days were required for this process to complete itself and, once the sarcoma became established, further propagation of the tumor resulted in complete elimination of the carcinoma with persistence of a pure sarcoma. In an exhaustive study of the problem, Haaland observed the same tissue transformation in transplanted breast tumors of mice. The reverse of this phenomenon has been reported by Nicholson.[14] In 1912, he inoculated the breast of a white female rat with sarcomatous tissue. Growth of a pure sarcoma occurred but, after reaching its maximum size, the tumor was seen to shrink. The excised specimen showed death of the sarcoma, while in its place a small malignant epithelial neoplasm had appeared. The origin of the carcinoma was thought by Nicholson to be from the lining of a sinus produced by his inoculation, an epithelial implant having been pushed into the deeper tissues by the needle. These experimental observations lend support to the possibility that a malignant lesion of epiblastic origin can stimulate adjacent mesoblastic elements to proliferate, and vice versa. Concerning the possibility that combination growths can originate from a single cell, widely divergent opinions prevail among pathologists so that no positive expression can be made at this time.

Classification and nomenclature of dual tumors of the breast are difficult and confusing because of the uncertainty regarding their etiology. Generally, they have been called either carcinosarcoma or sarcocarcinoma, depending upon which tissue element predominates in the microscopic sections. Harrington and Miller[15] proposed that mixed malignant lesions be designated according to the observer's conception as: (1) mixed growths or malignant teratomas, (2) carcinoma with secondary sarcoma, (3) sarcoma with secondary carcinoma, (4) carcinoma and sarcoma.

Tables I and II comprise a summary of the literature of thirty-two cases, reported by thirty authors, of breast tumors composed of more than one malignant element. Table I includes twenty-two cases of true mixed tumor wherein the neoplastic components are intimately blended with one another. Table II represents ten cases in which the individual malignant tissues are not intermingled but coexist simultaneously as independent tumors within the same breast. This review includes only those cases in which the tumor elements were composed of sarcoma and mammary carcinoma. All patients reported were

TABLE I

AUTHOR	DATE	AGE OF PATIENT (YR.)	TYPE OF NEOPLASM	METASTASES
Dorsch[20]	1896	43	Carcinoma and spindle-cell sarcoma; malignant elements blended	N. G.*
Kerberiou and Danel[21]	1897	55	Carcinoma and myxosarcoma; slight blending of malignant elements	Carcinoma only; axillary nodes
Schlagenhaufer[23]	1906	50	Carcinoma and giant-cell and spindle-cell sarcoma, partially blended	Both malignant elements, axillary nodes
Krompecher[24]	1908	36	Carcinoma and giant-cell sarcoma; intimate blending of both malignant elements	N. G.
Orth[25]	1910	40	Carcinoma and sarcoma intimately blended	N. G.
Pfeiffer[26]	1910	71	Carcinoma and spindle-cell sarcoma; intimate blending of both malignant elements	Carcinoma only; axillary nodes
Coenen[27]	1910	43	Carcinoma and spindle-cell sarcoma; intimate blending of both elements	Carcinoma only; axillary nodes; postoperative recurrence at 5 mo. of sarcoma only in axillary nodes
Secousse[28]	1912	67	Carcinoma and fibrosarcoma; intimate blending of both elements	N. G.
Waelle[30]	1913	50	Chondrosarcoma and carcinoma; blending of malignant elements	N. G.
Takano[31]	1914	49	Carcinoma and spindle-cell sarcoma; intimate blending of both types of neoplastic tissue	Carcinoma only; axillary nodes
Wehner[32]	1915	41	Spindle-cell sarcoma, scirrhus carcinoma, and squamous-cell epithelioma; intimate blending of all elements into "true mixed tumor"	N. G.
Hedrén[34]	1915	42	Spindle and giant-cell sarcoma and carcinoma; intimate blending of both malignant elements	None found
Harbitz[35]	1916	*	Giant-cell sarcoma and carcinoma; intimate blending of both malignant elements	N. G.
Wilensky[36]	1919	48	Round- and spindle-cell sarcoma intimately blended with carcinoma	N. G.
Kunsmüller[37]	1920	73	Spindle-cell sarcoma and carcinoma; intimate blending of both malignant elements	Sarcoma; lungs, pleura and ribs; no carcinoma
Jessup[38]	1923	34	Giant- and spindle-cell sarcoma intimately blended with carcinoma	Carcinoma only; axillary nodes
Kreibig[39]	1925	52	Case II, cylindrical and epidermoid carcinoma and spindle-cell sarcoma, intimately blended	Carcinoma only; axillary nodes
Biebl[40]	1927	62	Case I, round-, spindle-, and giant-cell sarcoma and carcinoma; intimate blending of elements	Original, none; postoperative recurrence in scar at 5 mo., of pure sarcoma

*N. G., Not given in original report.

TABLE I.—CONT'D

AUTHOR	DATE	AGE OF PATIENT (YR.)	TYPE OF NEOPLASM	METASTASES
Helwig[41]	1927	43	Carcinoma and giant-cell sarcoma intimately blended throughout breast	Both carcinoma and sarcoma, axillary nodes; postoperative recurrence in scar at 3 mo. of both elements
Kückens[42]	1928	48	Carcinoma and spindle-cell sarcoma; intimate blending of both malignant elements	N. G.
Pasternack and Wirth[43]	1936	60	"Adenoma acanthoma sarcomatodes," epidermoid carcinoma intimately blended with sarcomatous stroma; independent adenocarcinoma surrounded by normal stroma; no blending with other malignant elements	None found
Harrington and Miller[15]	1940	50	Spindle- and giant-cell sarcoma and carcinoma; intimate blending of both malignant elements	None found

women, no recorded instance being found of mixed carcinoma and sarcoma in the male breast. Not included in the collected cases are mixed breast tumors of sarcomatous and epidermoid carcinomatous composition. For detailed information about this variety of neoplasm the papers of Bouchut and Martin,[16] Lecène,[17] DeBoucaud and Pierre-Nadal,[18] and Cornil[19] may be consulted.

CASE REPORT

CASE 1 (Roper Hospital Case No. 111954).—A 10-year-old Negro girl entered the hospital Aug. 8, 1940, complaining of an enlargement of the left breast. Her mother stated that the patient developed a swelling within the affected breast "about the size of an egg" when she was 2 years old, the mass spontaneously disappearing within six months. The child experienced no further difficulty until five months prior to admission, at which time the same breast began to enlarge diffusely. Increase in size continued until, at the time of hospitalization, the breast resembled that of a fully developed young adult woman. There was no pain or tenderness of the affected breast and no history suggesting an inflammatory process. On a previous occasion, three months before admission, there occurred a white discharge from the nipple which persisted for only a day. No other nipple discharge of any sort was noted. The right breast remained undeveloped and was at no time a source of complaint. The child never had menstruated. The remaining history of her systems was normal. The mother thought that some weight loss had occurred but was uncertain of the amount. The family history revealed no known evidence of cancer and no other pertinent data. The past history included measles and chicken pox but revealed no organic ailments. Growth and development since birth had been normal.

Physical examination on admission showed a normally developed, fairly well-nourished girl. Temperature was 99° F.; blood pressure, 114/68; pulse, 100 per minute. The left breast was diffusely enlarged, measuring 11 by 9 cm., while

TABLE II

AUTHOR	DATE	AGE OF PATIENT (YR.)	TYPE OF NEOPLASM	METASTASES
Gould[22]	1901	56	Largely spindle-cell sarcoma; separate, independent growth of scirrhus carcinoma	N. G.*
Kettle[7]	1912	46	Separate neoplasms of carcinoma and fibrosarcoma blended only at point of contact of the two tumors	Original not given; postoperative recurrence at 3 yr. with generalized metastases of carcinoma only
Perrier[29]	1912	60	Spindle and giant-cell sarcoma and carcinoma; no intimate blending of elements	N. G.
Schwarz[9]	1913	50	Metastatic carcinoma (from opposite breast) associated with independent sarcoma; no blending	Carcinoma only; axillary nodes
Kennedy and Case[33]	1915	46	Carcinoma and spindle-cell sarcoma existing as separate independent tumors; no blending of elements	Carcinoma only; axillary nodes
Kreibig[39]	1925	50	Case 1, carcinoma and osteosarcoma growing independently; no blending of malignant elements	Carcinoma only; axillary nodes
Biebl[40]	1927	55	Case 2, polymorphic giant-cell sarcoma and medullary carcinoma existing as adjacent but separate independent neoplasms; no intermingling	None found
Lester[10]	1931	50	Postoperative recurrence in scar at 15 mo. of carcinoma associated with neurogenic sarcoma; independent, unrelated tumors with no blending of malignant elements	N. G.
Curphey[8]	1935	33	Carcinoma and spindle-cell sarcoma existing as adjacent, independent growth; no blending of malignant elements	Carcinoma in liver; no sarcoma
Mondor, Gauthier-Villars, and Gottesmann[44]	1936	49	Carcinoma and spindle-cell sarcoma in contact with each other but existing as separate unblended tumors	None found

*N.G., Not given in original report.

the right breast and nipple were normal. On palpation, the enlarged breast was found to be firm, somewhat elastic, and lobulated. The excess mammary tissue was not attached to the chest wall or to the overlying skin. Mobility of the entire breast was free in all directions, and there was no retraction of the nipple or its areola. There were numerous small discrete, firm, movable lymph nodes in the left axilla. One in particular was considerably larger than the others. Discretely enlarged lymph nodes were also noted in the opposite axilla, in the neck, and in both inguinal regions. Aside from marked hypertrophy of the tonsils, no other abnormalities were noted.

Routine laboratory studies of the urine and blood were normal. The blood Wassermann and Kline tests were negative. X-ray studies of the chest, vertebral column, and long bones showed no abnormalities and there was no radiographic

evidence of pituitary tumor. The basal metabolic rate was minus 16 per cent. A Friedman modification of the Aschheim-Zondek reaction was negative.

It was felt that enlargement of the affected breast was due to simple hyperplasia, possibly of endocrine origin, although no specific disorders of the endocrine system could be found. Accordingly, a simple mastectomy was done through transverse elliptical incisions, and the entire breast removed, along with the largest of the axillary lymphoid masses, which was readily accessible near the lateral end of the operative wound. The entire mammary mass appeared to be encapsulated and was quite easily stripped from the underlying pectoral fascia. An axillary dissection was not done. Postoperative convalescence was uneventful.

Pathologic Description.—Microscopic sections of the breast revealed a highly malignant connective tissue neoplasm of spindle-cell type. The cellular elements were arranged in swirling bands (Figs. 1 and 2) and varied in appearance from slender, elongated structures to broad, anaplastic, ribbonlike masses of cytoplasm

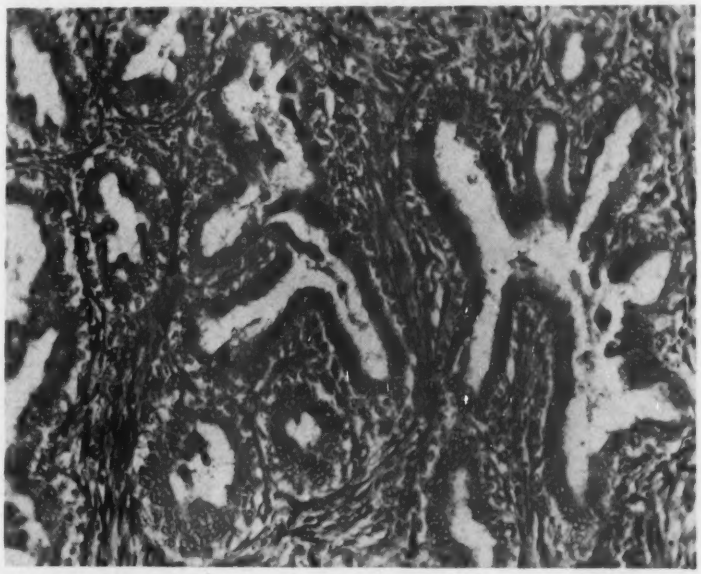


Fig. 1.—Bands of spindle cells arranged about atypical glandular elements (×200).

(Fig. 3). The large ovoid and spindle-shaped nuclei showed a pronounced hyperchromatic character. Tumor giant cells and atypical mitotic figures were numerous and emphasized the high grade of malignancy (Figs. 3 and 4). Scattered throughout the tumor were many branching glandular elements of atypical appearance. Hyperplasia of the lining epithelium was well defined and papillary ingrowth was a prominent feature (Figs. 1 and 2). In spite of this proliferative activity, there was no specific evidence in the many sections taken from the breast tissue itself that the epithelial portion of the tumor was malignant, although a few mitotic figures were seen among the reduplicated epithelial cells. Sections of the removed axillary node, however, showed invasion of the lymphoid tissue in its subcapsular zone by the same glandular elements noted in the primary tumor, but none of the sarcomatous element was found.* Their anatomic arrangement was typical of early metastatic adenocarcinoma, the parent glandular structure being maintained intact. The histologic diagnosis was spindle-cell sarcoma and adenocarcinoma with early metastases of the carcinomatous element to the axillary lymph nodes.

*Sections of the lymph node are not available for photomicrographs.

Postoperative Course.—Shortly after operation, deep x-ray therapy was begun. The patient received a total of 9,000 R (measured in air), administered to six fields over a period of six weeks. Ten months after operation, she was readmitted to the hospital for study. Her progress had been highly satisfactory and she had

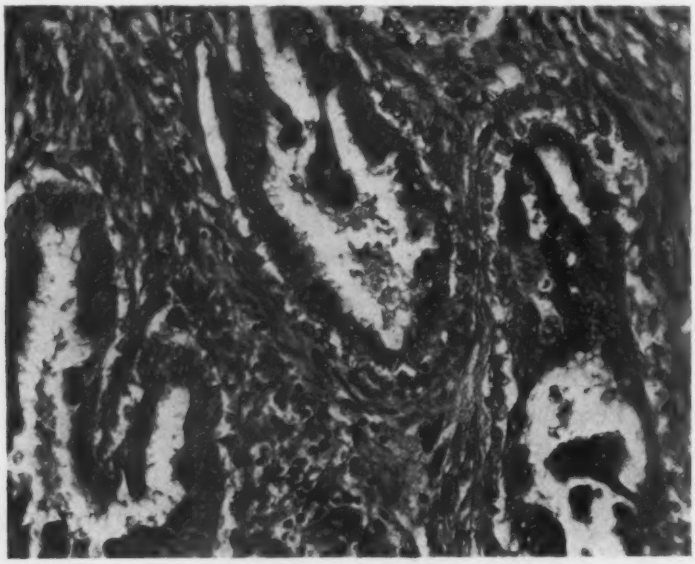


Fig. 2.—Glandular elements showing marked hyperplasia of the epithelium with papillary invaginations (×300).

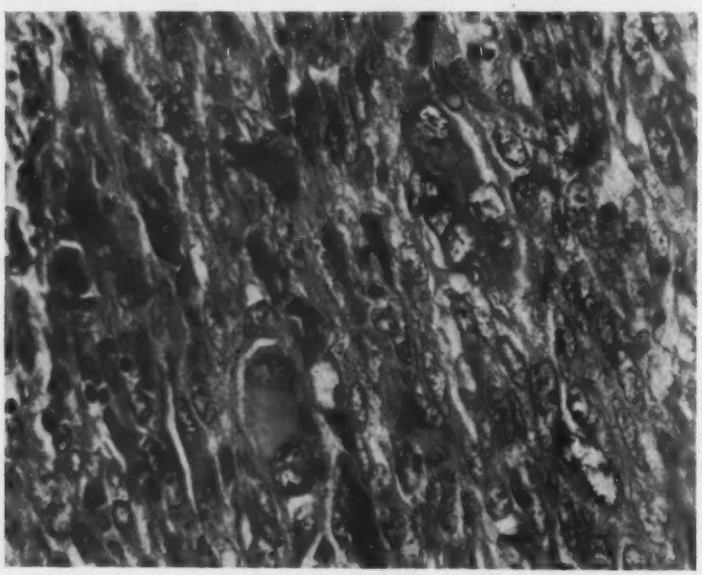


Fig. 3.—Large nuclei, tumor giant cells, and broad anaplastic chromatin masses of the mesoblastic component (×500).

led a normal, uneventful existence. Radiologic studies of the lungs, thoracic cage, vertebral column, and long bones showed no evidence of metastatic malignancy. The operative scar was soft and pliable and freely movable over the chest wall. Developmental changes of puberty were noted and appeared quite normal, but the patient had not menstruated to this time. Her weight was 91 pounds. In August,

1942, two years after operation, further roentgenologic studies of the chest and vertebral column were found to be entirely normal. In March, 1943, thirty-one months postoperative, the patient was seen again. Menstruation had begun the previous month (at the age of 12½ years). As on previous occasions, the history and physical examination revealed no abnormalities and her condition appeared to be excellent; weight was 99 pounds. In November, 1943, three years and three months postoperative, correspondence from the child's mother stated that the patient was "getting along fine" and reported her weight as 103 pounds. A similar report was received in June, 1944, three years and ten months postoperative, stating that the child weighed 110 pounds and that her health was excellent.

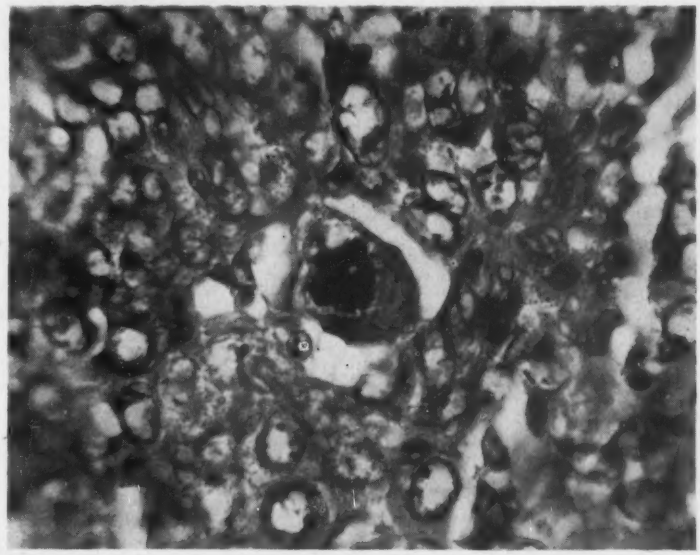


Fig. 4.—Large atypical mitotic figure of the sarcomatous element (×750).

DISCUSSION

Consideration of the foregoing case focuses attention on the following points of interest: (1) the nature of the tumor, (2) the age of the patient, and (3) the method of treatment.

Regarding classification of the tumor, it is desirable to avoid such terms as carcinosarcomatodes, carcinosarcoma, and sarcocarcinoma which have been employed to indicate the relative time of appearance of the different malignant components of a dual tumor, as well as a preponderance of one element over the other. Actually, the neoplasm described consists of two well-defined individual malignant tissues. Inasmuch as the pathogenesis of such a growth is unknown, little is to be gained by speculation as to the relative time factors in the development of each component. Therefore, for the purpose of clarity, it is suggested that the neoplasm be called a mixed sarcoma and adenocarcinoma. The word "mixed" is an important qualifying descriptive factor designed to differentiate the tumor from a situation where sarcomatous and carcinomatous growths exist as separate, independent neoplasms in the same breast.

Concerning the patient's age, the development of a dual mammary neoplasm at 10 years is extraordinary. Only four authentic cases of carcinoma of the breast have been reported as occurring before puberty. The ages were 11 years (Thompson[45]), 11 years (Eliot[46]), 12 years (Levings[47]), and 10 years (Sears and Schlesinger[48]). It is believed that this report constitutes the only recorded instance of a combined sarcoma and carcinoma of the breast of a child.

The method of treatment employed in this case is open to question. While removal of the breast was considered necessary, it was the impression of several examiners who saw the patient before operation that the lesion was benign, most probably mammary hyperplasia of an extreme degree. Accordingly, a simple mastectomy was done without frozen section study. The latter procedure is of established value and it should be employed in all questionable neoplasms of the breast coming to operation. However, the histologic nature of the tumor was such that frozen section would have demonstrated no more than the sarcomatous element. In general, mammary sarcomas rarely invade axillary lymph nodes so that axillary dissection is generally considered illogical in the operative treatment of this lesion, removal of the breast and pectoral muscles being the procedure of choice. This being true, the actual surgical management of the case conformed to the general principles of treatment of sarcoma of the breast, with the exception of removing the pectoral muscles.

Discovery of the carcinomatous factor was made only after sections of the axillary lymphoid tissue were examined. The involved lymph node was excised only because of its proximity to the incision, no attempt being made to dissect the axillary contents. Such being the case, the question arose as to the advisability of a second operation for removal of the pectoral muscles and the lymphoid structures of the axilla and supraclavicular space, after discovering the metastatic carcinoma. Probably such a radical procedure should have been carried out, but factors beyond control prevented it. In spite of the patient's relatively long survival, criticism of the conservative treatment employed is justifiable.

Regarding the uneventful postoperative course, now of three years and ten months' duration, one can only speculate upon the explanation. Several possibilities present themselves. It is quite likely that the entire sarcoma was removed, inasmuch as it appeared to be securely encapsulated. It is conceivable that the carcinoma, which was judged to be early by microscopic study, had metastasized to only a single axillary node, which happened by pure chance to be the one removed. It is probable that postoperative deep x-ray therapy played a responsible part in maintaining the patient's health by holding in abeyance any remaining malignant elements, and that the conservative method of treatment employed makes a permanent cure unlikely.

SUMMARY

1. A brief discussion of mixed carcinoma and sarcoma of the breast is presented from both clinical and experimental viewpoints.

2. A review of reported cases is prepared in tabulated form.

3. An unusual case of mixed sarcoma and adenocarcinoma in a 10-year-old Negro girl is reported in detail, believed to be the first of its kind recorded in a child.

4. Discussion of the case from three standpoints is included: (1) the nature of the tumor, (2) the patient's age, and (3) the method of treatment regarding prognosis.

Due appreciation is hereby expressed to Dr. H. R. Pratt-Thomas, of the Department of Pathology, for his invaluable help in the preparation of this report.

REFERENCES

1. Wells, H. G.: Multiple Primary Malignant Tumors: Report of a Primary Sarco-Carcinoma in the Thyroid of a Dog, With mixed Sarcomatous and Carcinomatous Metastases, J. Path. & Bact. **7**: 357, 1901.
2. Loeb, Leo: Mixed Tumors of the Thyroid Gland, Am. J. M. Sc. **125**: 243, 1903.
3. Major, R. H.: Multiple Primary Malignant Tumors With Report of a Case of Carcinoma and Sarcoma in the Same Individual, Bull. Johns Hopkins Hosp. **29**: 223, 1918.
4. Burke, M.: Multiple Primary Cancers, Am. J. Cancer **27**: 316, 1936.
5. Hurt, H. H., and Broders, A. C.: Multiple Malignant Neoplasms, J. Lab. & Clin. Med. **18**: 756, 1933.
6. Wehrbein, H. L., and Weber, J. J.: Multiple Primary Malignant Lesions, Am. J. Surg. **61**: 143, 1943.
7. Kettle, E. H.: Carcinoma and Sarcoma of the Same Breast, Lancet **2**: 750, 1912.
8. Curphey, W. C.: Primary Spindle-Cell Sarcoma Associated With a Primary Scirrhus Carcinoma, J. Kansas M. Soc. **36**: 412, 1935.
9. Schwarz, Emil: Carcinoma and Sarcoma Mammae, Am. J. Obst. **68**: 752, 1913.
10. Lester, C. W.: Sarcoma Associated With Metastases From Breast Carcinoma, Am. J. Cancer **15**: 850, 1931.
11. Ehrlich, P., and Apolant, H.: Beobachtungen über maligne Mäusetumoren, Berl. Klin. Wchnschr. **2**: 871, 1905.
12. Haaland, M.: Contributions to the Study of the Development of Sarcoma Under Experimental Conditions, Third Scientific Report of the Investigations of the Imperial Cancer Research Fund, 1908, p. 175.
13. Russell, B. R. G.: Sarcoma Development During the Propagation of a Hemorrhagic Adenocarcinoma of the Mamma of the Mouse, J. Path. & Bacteriol. **14**: 344, 1910.
14. Nicholson, G. W.: A Small Carcinoma in Association With a Transplanted Sarcoma in a Rat, J. Path. & Bacteriol. **16**: 518, 1911-12.
15. Harrington, S. W., and Miller, J. M.: A Mixed Tumor (Carcinosarcoma) of the Breast, SURGERY **7**: 122, 1940.
16. Bouchut, L., and Martin, J. F.: A propos d'un cas de tumeur complexe du sein, Lyon chirurg. **18**: 425, 1921.
17. Lecène, P.: Tumeur mixte du sein chez la femme (sarcome à myéloplaxes et épithéliome pavimenteux), Bull. et mém Soc. anat. de Paris **79**: 698, 1904.
18. De Boucaud, and Pierre-Nadal: Tumeur mixte du sein à formations malpighiennes, Bull. de l'Ass. franç. p. l'étude du cancer **4**: 46, 1911.
19. Cornil, V.: Les tumeurs du sein, Paris, 1908, Baillière et cie.
20. Dorsch: Ueber Karzinom und Sarkom derselben Mamma, Inaugural Dissertation, Wurzburg, 1896. Quoted by Kückens.[42]
21. Kerberiou, and Danel: Sarco-épithéliome kystique de sein, J. d. sc. méd. de Lille **1**: 175, 1897.
22. Gould, P.: Carcinoma and Sarcoma of the Same Breast. The Middlesex Hospital Reports for the Year 1900, p. 81.

23. Schlagenhaufer: Carcinom und Reisenzellsarkom derselben Mamma, Centralbl. f. allg. Path. u. path. Anat. **17**: 385, 1906.
24. Krompecher, E.: Ueber die Beziehungen zwichen Epithel und Bindegewebe bei den Mischgeschwültzen der Haut und der Speicheldrüsen und über das Enstehen der Karcinosarkome, Beitr. z. path. Anat. u. z. allg. Path. **44**: 88, 1908.
25. Orth, J.: Bericht über das Leichenhaus des Charité-Krankenhauses für das Jahr 1909, Charité-Ann., Berlin **34**: 357, 1910.
26. Pfeiffer, D. B.: Mixed Tumor of the Breast, With Malignant Changes Both in the Connective Tissue and Epithelium, Proc. Path. Soc. Phila. **13**: 267, 1910.
27. Coenen, H.: Ueber Mutationsgeschwültse und ihre Stellung in onkologischen System, Beitr. z. klin. Chir. **68**: 605, 1910.
28. Secousse, M.: Sur un cas de fibro-sarcome kystique de la mammelle s'accompagnant de points carcinomateux et à contenu gelatineux, J. de méd. de Bordeaux **42**: 791, 1912.
29. Perrier, H.: Les sarco-carcinomes de sein, Rev. méd. de la Suisse Rom. **32**: 447, 1912.
30. Waelle: Carcinoms Sarcomatodes der Mamma, Inaugural Dissertation, Zurich, 1913. Quoted by Kückens.[42]
31. Takano, N.: Ueber das Carcinoma Sarcomatodes der Mamma, Arch. f. klin. Chir. **103**: 155, 1914.
32. Wehner, E.: Ein Beitrag zur Frage der Karcino-sarkom unter Mitteilung eines Mammatumors, Frankfurt. Ztschr. f. Patho., Wiesb. **16**: 167, 1915.
33. Kennedy, J. W., and Case, E. A.: Sarcoma and Carcinoma of the Same Mammary Gland, Proc. Path. Soc. Phila. **18**: 40, 1915.
34. Hedrén, G.: Sarkocarcinom der Mamma, Zentralbl. f. allg. Pathol. u. path. Anat. **26**: 265, 1915.
35. Harbitz, F.: Über das gleichzeitige Auftreten mehrerer selbständig wachsender ("multipler") Geschwültze, Beitr. z. path. Anat. u. z. allg. Path. **62**: 503, 1916.
36. Wilensky, A. O.: A Case of Carcinosarcoma of the Breast, Proc. N. York Path. Soc. **19**: 113, 1919.
37. Kunsmüller: Ein Karzinomsarcom der Mamma, Inaugural Dissertation, Breslau, 1920. Quoted by Kückens.[42]
38. Jessup, D. S. D.: Giant Cell Sarcoma and Carcinoma in the Same Breast, Proc. N. York Path. Soc. **23**: 21, 1923.
39. Kreibig, W.: Zur Kenntnis seltener Geschwulstformen der weiblichen Brustdrüse, Virchows Arch. f. path. Anat. **256**: 649, 1925.
40. Biebl, M.: Das Mammasarkom und seine Beziehungen zur Fibrosis Mammae wie zu den gutartigen Mammageschwültzen, Beitr. z. klin. Chir. **140**: 52, 1927.
41. Helwig, F. C.: Carcinoma of the Breast Combined With a Giant Cell Sarcoma, Arch. Path. & Lab. Med. **4**: 162, 1927.
42. Kückens, H.: Ueber seltenere Formen von Mammageschwülsten, Beitr. z. path. Anat. u. z. allg. Path., Jena **80**: 116, 1928.
43. Pasternack, J. G., and Wirth, J. E.: Adeno-acanthoma Sarcomatodes of the Mammary Gland; Report of a Case With a Critical Review of the Literature of Squamous Epithelium in Intramammary Tumors, Am. J. Path. **12**: 423, 1936.
44. Mondor, H., Gauthier-Villars, P., and Gottesmann, H.: Carcinosarcome du sein, Ann. d'anat. path. **13**: 783, 1936.
45. Thompson: Quoted by Deaver, J. B., and McFarland, J.: The Breast; Its Anomalies, Its Diseases, and Their Treatment, Philadelphia, 1917, The Blakiston Company, p. 514.
46. Eliot, E.: Breast Cancer in Young Women, Ann. Surg. **53**: 726, 1911.
47. Levings, A. H.: Carcinoma of the Mammary Gland in a Girl 12 Years Old, Am. J. Surg. **31**: 29, 1917.
48. Sears, J. B., and Schlesinger, M. J.: Carcinoma of the Breast in a 10 Year Old Girl, New England J. Med. **223**: 760, 1940.

BOECK'S SARCOID

Report of a Case Involving the Stomach

Major Ira Gore, and Lieutenant Colonel Alphonsus M. McCarthy,
Medical Corps, Army of the United States

PRIOR to 1936, despite a not inconsiderable discussion in the foreign literature, Boeck's sarcoid was a relatively unknown subject to American medicine. Since that time several reviews[2, 3, 6, 8] have brought the condition to the attention of the internist. The surgeon's only contact with it was to provide the biopsy by which the diagnosis is established. Although the disease is not a common one, over a four-year period twenty-three new cases were recognized in a clinic which had become acutely aware of its manifestations.[2] Previously, this condition has not been regarded as surgically important. For this reason it is deemed appropriate to present a brief review and to report a case demonstrating that important surgical complications may develop.

Boeck's sarcoid has come to be regarded as a relatively benign disease of obscure etiology having a predilection for lymphoid tissue[1] but capable of involving any tissue in the body.[2] Despite this potentiality a large proportion of the cases reported are characterized by skin lesions, regional or generalized lymph node enlargement, a stringy or miliary infiltration of the lungs, and cystic changes in the long bones of the hands and feet. In each of these structures the pathologic unit identifying the process is the "hard tubercle" formed of a nodular aggregation of plump polygonal, acidophilic epithelioid cells identical with those found in tuberculosis. Differentiating it from the latter are the almost total absence of caseation, the scarcity of surrounding inflammatory reaction, the absence of demonstrable organisms, and the relative scarcity of Langhans' giant cells. Regarding the latter, the occasional presence of deeply basophilic laminated inclusions in the giant cells is regarded as almost pathognomonic.[1, 2] Guinea pig inoculations of such tissue produce no characteristic reaction. In 60 to 70 per cent of cases there is a negative or very weak tuberculin skin reaction. In the skin, these sarcoid lesions produce sharply defined nodular or papular lesions of variable size, frequently of reddish color involving the skin of the face, extremities, or both. It is of historical interest that this condition was first described as a dermatologic entity.[3] Although Hutchinson in 1875, Besnier in 1889, and Tenneson in 1892 described undoubted instances of the disease, it was not established as a clear-cut entity until Boeck, in 1899, described the pathologic alterations in the skin. Although Boeck[4] noted enlargement of the cubital, femoral, and axillary nodes in his original case and subsequently described involvement of the

Received for publication, June 1, 1944.

mucosae of the conjunctivae, nose, genital tract, and bronchi, the manifestations of the disease were not generally regarded as more than skin deep until Schaumann, in 1914, emphasized and demonstrated microscopically involvement of the lymph nodes by lesions identical with those in the skin. In his subsequent writings Schaumann[1] stressed the predilection of the process for lymphoid tissue and termed it lymphogranuloma benignum to distinguish it from lymphogranuloma malignum, Hodgkin's disease. In 1915, Kuznitsky and Bittorf focused attention on the pulmonary manifestations and in 1919 Jungling,[5] although there had been prior reports, demonstrated and proved histologically the relationship of the cystic changes (osteitis tuberculosa multiplex cystica) in the long bones of the hands to the skin lesions. Uveoparotid fever described by Heerfordt, 1909, was demonstrated to be due to sarcoid involvement of the parotid gland and uveal tract by Bruins Slot in 1936 and by Longcope and Pierson in 1937.[6] Less frequently sarcoid involvement of the spleen and liver have simulated Banti's syndrome,[7] involvement of the pituitary has produced diabetes insipidus, myocardial involvement has been responsible in several cases for prominent cardiovascular symptoms, and destruction of the testes has produced eunuchism.

From the first the disease was recognized as a benign one which, as Boeck expressed it, "disappears under arsenic therapy or perhaps spontaneously." Involution of skin lesions results "in a loss of substance in the skin which may be white on the face, yellow on the back and darker at the periphery on the legs."[4] Pathologically, involution is expressed by fibrosis of the nodular lesions. Frequently the fibrous tissue stains for amyloid. The location and character of the scarring supported by a suggestive clinical history is often sufficient for a positive pathologic diagnosis.[8]

Large numbers of case reports testify to the benignity of the disease. As Longcope expressed it, "symptoms when they exist are caused primarily by the mechanical interference with the function of organs rather than any form of intoxication."[2] Irregular fever may be present during the clinical course, there is a tendency toward eosinophilia, and hyperglobulinemia is frequently present. Involvement of vital organs by even an involuting process may result in permanent sequelae or perhaps death. Schaumann emphasized the circulatory disturbance ensuing from extensive pulmonary disease, while more recently Longcope and Fisher[9] reported several patients with direct myocardial infiltration. Permanent visual impairment may ensue from disease of the uveal tract, and diabetes insipidus has been reported from pituitary and hypothalamic involvement. Of the twenty-five autopsies reported to 1941,[2] active tuberculosis had played a role in causing the death of eight patients. Whether this fact is to be regarded as etiologically significant is controversial, still a marked predisposition toward such a

terminus must be admitted. Kissmeyer, who studied the disease extensively, states that clinical tuberculosis develops in less than 10 per cent of the cases.[6]

Although lesions have been found in almost every tissue of the body, clinical symptoms pointing to involvement of the intestinal tract have not previously been reported. In Tillgren's patient with diabetes insipidus terminating with tuberculous peritonitis,[1, 10] the gastric mucosa was atrophic and there were numbers of submucosal fibrotic nodules; there had been no symptoms to suggest such gastric involvement. Rakov and Taylor[11] described a patient with abdominal symptoms presenting at laparotomy miliary involvement of the liver and perigastric nodes. Lenartowicz's[12] patient had truly tuberculous miliary lesions of the ileum and cecum rather than sarcoid lesions. In a case report by Bernstein, Konzlemann, and Sidlick,[13] unexplained abdominal pain during the terminal stages of a fatal illness was ascribed to multiple ulcerations present in the ileum. These were considered by Bernstein and co-workers to be due to sarcoid but their photomicrographs are far from convincing.

Because of its uniqueness therefore, the following case is reported.

CASE REPORT

Illness at Time of Admission.—This 26-year-old soldier first noticed stomach trouble in June, 1941. His complaints consisted of burning and sometimes griping pains in the epigastrium after meals. Symptoms were associated with belching and eructation of bits of food and bitter, hot slimy material. At his organizational dispensary he was given pills and powders which for a while gave him moderate relief. Soft foods such as bread and milk made his symptoms less severe; but, from July until December, 1941, because he was on maneuvers, he was obliged to eat field rations. His symptoms gradually became more persistent. In April, 1942, he was transferred to a southern camp. There he reported to the dispensary regularly but medication provided no relief. He noticed a loss in weight from 186 pounds in May, 1942, to 168 pounds on Dec. 7, 1942. In September, 1942, he began to vomit occasionally following meals. Postprandial vomiting became more frequent until at the time of hospitalization, Dec. 7, 1942, he could retain very little. The epigastric pain at this time was more or less continuous, both day and night. He ate with reluctance because a few mouthfuls gave him the added discomforts of distention, nausea, and regurgitation.

Past History.—His past history revealed no familial history of tuberculosis or cancer. In 1934 he had symptoms indicating gonorrheal urethritis, and a dorsal slit was required about this time because of phimosis. Since May, 1942, he has had venereal warts of the prepuce. There was no history of skin rash, sores, or adenopathy.

Physical Examination.—Examination revealed a moderately debilitated but well-developed man in no acute distress. Temperature, pulse, and respiration were normal. Blood pressure was 160/100. Positive findings were limited to moderate emaciation, veneral warts of the prepuce, and moderately enlarged inguinal lymph nodes. Blood count on admission showed a hemoglobin of 75 per cent; the red cells numbered 4.2 million, the white 7,600; differential was normal. Dark field examinations of the preputial lesion were negative on three successive days.

Hospital Course.—Shortly after admission the preputial venereal warts were fulgurated. The blood Wassermann reaction, Dec. 10, 1942, was negative. Radiologic examination of the gastrointestinal tract revealed a persistent cone-shaped

deformity of the pyloric antrum through which only very shallow persistaltic waves traveled; this rigidity suggested an intramural infiltration of some kind, probably neoplastic in nature (Fig. 1). There was no evidence of ulceration or of four-hour gastric retention. Stools were negative for occult blood. January 15, 23, and 25, three successive positive Wassermann and Kahn serologic reactions were reported and syphilis of the stomach was considered even though the radiologic findings were not suggestive of this disease. (Quantitative Kahn tests showed an increasing titer from less than 10 units on January 15, to 10 units on January 23, and 40 units on February 8.) Jan. 27, 1943, antisyphilitic treatment was instituted as a therapeutic test. Three doses of neoarsphenamine, one of bismuth, and one of mapharsen were given prior to Feb. 10, 1943. On this date the radiologic appearance of

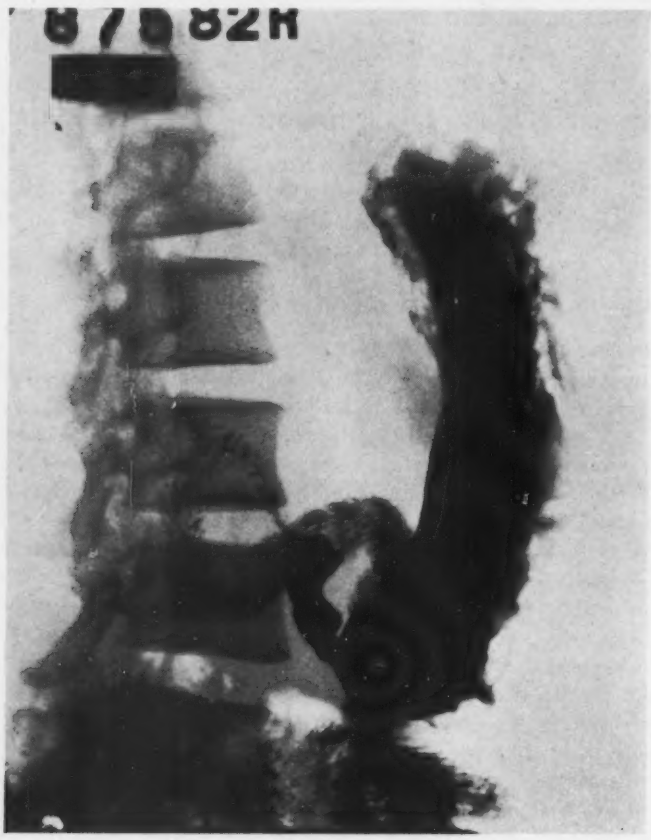


Fig. 1.—Preoperative x-ray picture illustrating the deformity of the stomach antrum.

the stomach showed persistent, "possibly increased" stenosis of the pyloric antrum of the stomach. Gastric analyses showed an absence of free hydrochloric acid after histamine, total acidity only reaching a maximum of 20 units. Other laboratory findings were essentially negative. The lungs were clear to x-ray. Because of failure to respond to antisyphilitic therapy, the impression at this time was that the patient had a gastric neoplasm, and he was transferred to the surgical service for exploratory laparotomy. The latter was performed, Feb. 23, 1943. Up to this date the patient had received a total of four doses of neoarsphenamine, three of mapharsen, and three of bismuth.

Operative Findings.—Laparotomy revealed a diffuse doughy thickening of the pyloric stomach. Both the anterior and posterior walls were involved as well as

the greater curvature. The lymph nodes along the omental attachment were markedly enlarged; the other viscera appeared normal. Biopsies of the thickened stomach wall and of an enlarged lymph node were taken for frozen section. These revealed the inflammatory nature of the lesion, a provisional diagnosis of gastric tuberculosis or sarcoid disease being made; a gastric resection was performed with Balfour-Polya type of anterior loop anastomosis. Postoperative convalescence was uncomplicated. Tuberculin tests with purified protein derivative were negative

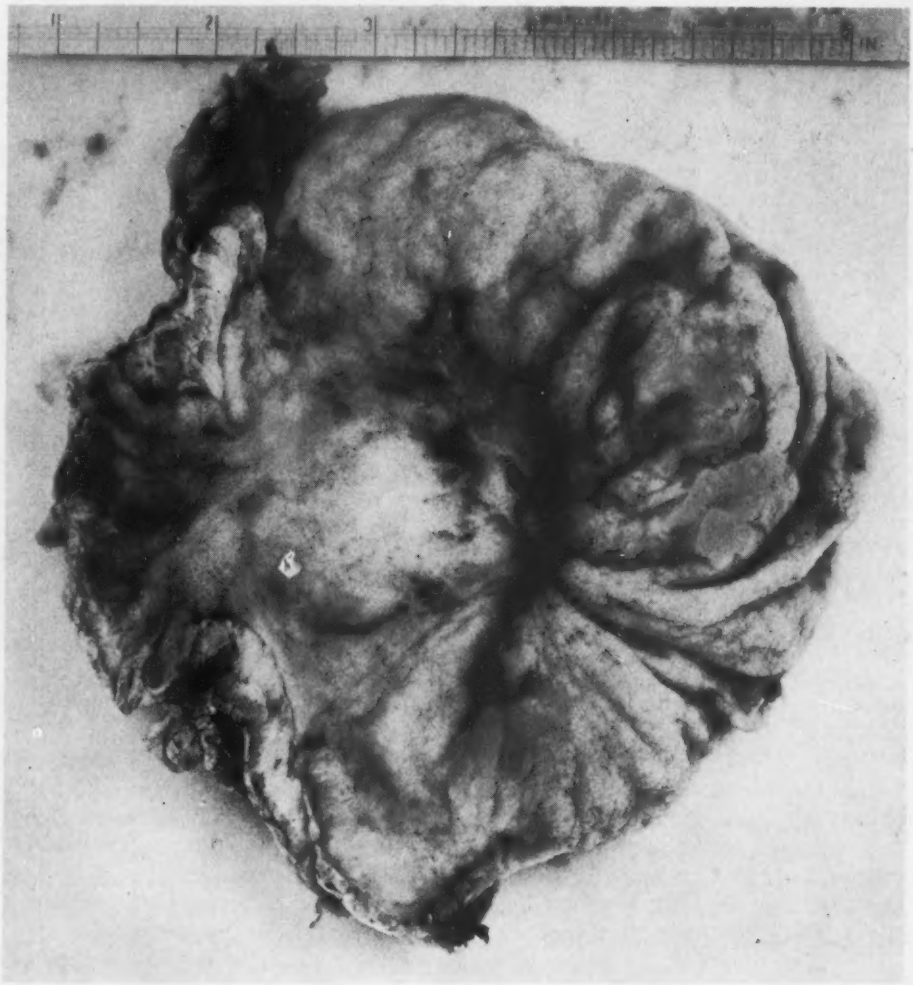


Fig. 2.—The mucosal aspect of the surgically excised portion of the stomach. The specimen has been opened along the lesser curvature; the greater curvature lies transversely straddled by a shallow crescentic ulcer. The proximal portion lies to the right, while the pyloric extremity lies to the left.

to the second strength. X-ray pictures showed no bony changes in the metacarpals or metatarsals and an inguinal lymph node presented only inflammatory hyperplasia. April 28, 1943, x-ray studies revealed an adequately functioning gastrojejunal anastomosis. Frequent feedings were necessary because of the small gastric capacity; he slowly gained weight. Intensive antisyphilitic treatment was continued and subsequent to May 27, 1943, the serology on four occasions was negative. June 3, gastric analysis showed an absence of free HCl.

Pathologic Report.—(S-254-43, A. M. M. Acc. 90296.)

Gross: The specimen consisted of a large segment of the gastric antrum measuring 8 cm. along the lesser curvature and 12 cm. along the greater curvature. On the anterior surface about 8 cm. proximal to the pyloric extremity there was a 4 cm., recently sutured linear incision covered with a small omental tag; this apparently was the seat of the biopsy. The serosal surface was shiny and translucent. However, toward the attachment of the omentum numbers of tiny slightly elevated translucent nodules were evident. Palpation revealed extensive thickening and induration of a rather large area on the greater curvature at about the mid-portion of the specimen. The specimen was opened along the lesser curvature (Fig. 2).

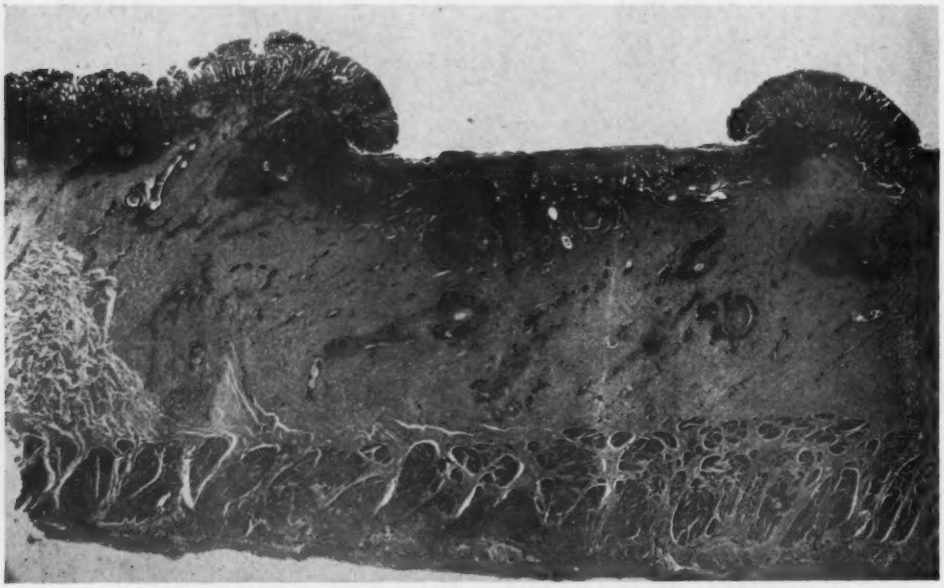


Fig. 3.—Photomicrograph through the stomach wall illustrating the marked thickening, the shallow mucosal ulceration, prominent endarteritic changes, and small pale nodules just below the mucosa to the left of the ulcer. (×10. U. S. Army Medical Museum.)

On the mucosal surface straddling the greater curvature 8 cm. proximal to the pyloric end, there was a crescentic, moderately deep ulceration. It measured 5 cm. in length and varied in width from 1 to 2 cm. The biopsy described externally evidently included the anterior pole of the ulcer, since in the operative specimen this part was markedly narrowed by the repairing suture. Proximal to the ulcer the mucosal folds were thickened and formed a sharply marginated overhanging wall. There was a slight tendency for puckering of the folds in the direction of the ulcer. The distal margin of the ulcer was comparatively poorly defined. Section of the stomach wall showed marked scarring and thickening of the submucosal layer underlying the ulcer site and extending toward the pylorus. At places along this line the gastric wall measured 2 cm. in thickness. The muscularis was intact and hyperplastic (Fig. 3).

Accompanying the specimen was a moderately enlarged lymph node removed from the omentum. The node measured 3 by 2 by 1.5 cm. and its capsule was thin and intact. Section revealed a yellowish-pink homogeneous surface.

Microscopic (Figs. 3 and 4).—Sections taken from the pyloric portion of the stomach showed an extensive round- and plasma-cell infiltration of the mucosa. The glandular epithelium showed variable cystic changes. There was moderate atrophy toward the pylorus where small areas of intestinal metaplasia were present.

The ulceration noted grossly barely penetrated the muscularis mucosae. A small quantity of purulent exudate was noted on its surface. The ulcer bed consisted of a rather thin layer of chronically inflamed granulation tissue. The underlying submucosa was markedly edematous and moderately scarred. The submucosal vessels showed rather marked endarteritic changes. Heavy mantles of round and plasma cells accompanied the vessels. In the mucosa and superficial submucosa adjacent to the ulcer there were nodular aggregates of epithelioid cells. These were unassociated with caseation or necrosis, and giant cells were rare. The muscularis was thickened by scar tissue and round-cell infiltration. The serosal surface contained a number of small lymphoid nodules in the centers of which epithelioid cells and an occasional Langhans' type giant cell were found; concentric laminated basophilic giant cell inclusions were demonstrable.

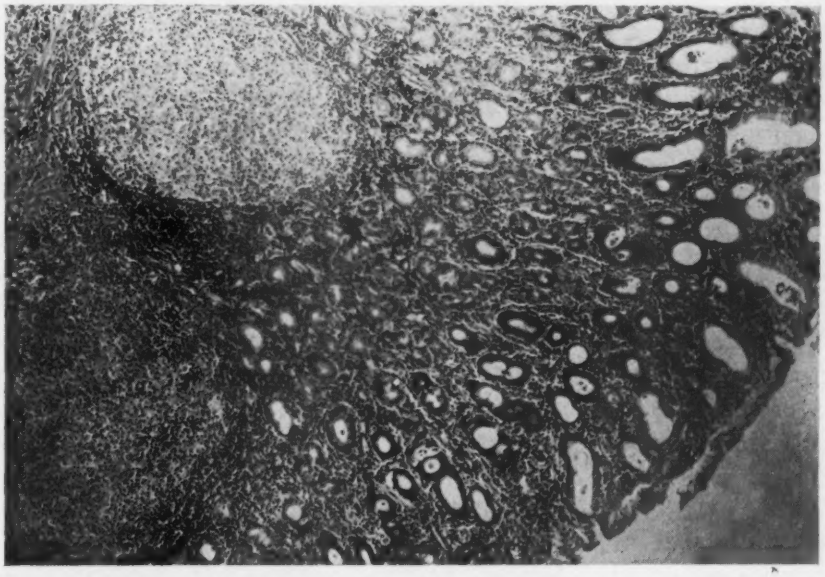


Fig. 4.—Gastric mucosa demonstrating nodular aggregates of epithelioid cells lying, in this instance, just above the muscularis mucosae. Note also the diffuse lymphocytic infiltrate and the glandular changes which signify chronic gastritis. (×100. U. S. Army Medical Museum.)

Sections taken from the lymph node exhibited similar nodular clusters of epithelioid cells. Again there was no necrosis, and giant cells were rare. There was a rather marked tendency toward hyaline scarring. The surrounding nodal parenchyma was hyperplastic and contained large numbers of plasma cells. The sinus endothelium was hyperplastic. Acid-fast bacilli were not demonstrable histologically or in digests and concentrates of portions of the specimen.

Diagnosis.—(1) Boeck's sarcoid of the stomach and lymph node and (2) subacute ulceration of the pyloric stomach.

We are aware of only one other case of gastric sarcoid (unpublished), presented by Dr. Fred Stewart to a surgical pathology conference of the New York State Laboratory Association in November, 1942.

DISCUSSION

As has been intimated, the preoperative diagnoses considered were peptic ulcer, gastric syphilis, and gastric neoplasm. Ulceration was understandably not demonstrated by x-ray since the ulcer was shallow and its position on the greater curvature did not lend itself to easy

demonstration. Furthermore, the presence of achlorhydria, the position of the lesion, and the lack of melena appeared to corroborate the negative roentgenologic findings. Peptic ulceration was therefore considered unlikely.

Gastric syphilis was considered a likely possibility because of a rising serologic titer, the relative youth of the patient, and the position of the lesion in the distal portion of the stomach.[14, 15] However, gastric syphilis is considered to be a manifestation of the tertiary phase of the disease, and in this case, although a history of a primary lesion is absent the change in serologic reaction from negative to positive, the consistent rise in serologic titer associated therewith, and the relatively prompt return to seronegativity under arsenotherapy all would indicate this to be certainly not late syphilis. Nonetheless, it was considered advisable to institute a therapeutic test of antisyphilitic treatment. There was no response to a short intensive course and after four weeks laparotomy was performed, the presumptive diagnosis being gastric neoplasm.

At operation, frozen sections ruled out a neoplastic process but resection was considered advisable since the lesion appeared to be progressing clinically. As the microphotographs (Figs. 3 and 4) demonstrate, the distinctive lesions of sarcoid are present in addition to secondary ulceration and rather extensive nonspecific productive inflammatory response. The prominence of the endarteritic changes and of the perivascular cellular infiltrate is suggestive of a syphilitic lesion but these processes are also commonly present in nonspecific ulceration. Endophlebitis, whose diagnostic value in syphilis has been demonstrated by Williams and Kimmelstiel,[15] could not be shown. Supported by the clinical features and course already described, the microscopic picture was considered not to represent syphilis.

From the first, one of the striking diagnostic features of Boeck's sarcoid was the comparative lack of surrounding inflammation. However, the mere mechanical presence of the sarcoid nodules in a mucosal surface subject to repeated physiologic trauma is felt sufficient to invoke an inflammatory response as in this case. Presumably, ulceration occurred secondarily, an impression substantiated by Hebbel's[16] work on chronic gastritis and ulceration.

It is not possible to draw any conclusions as to treatment from one case of "surgical" sarcoid disease. Each case must be individualized. Although there is a strong tendency toward spontaneous resolution in the primary disease, it is the secondary complication making the case "surgical" that must be gauged in treating the patient.

REFERENCES

1. Schaumann, J.: Benign Lymphogranuloma and Its Cutaneous Manifestations, Brit. J. Dermat. 36: 515, 1924.
Idem: Lymphogranulomatosis Benigna in the Light of Prolonged Clinical Observations and Autopsy Findings, Brit. J. Dermat. 48: 399, 1936.

Idem: On the Nature of Certain Peculiar Corpuscles Present in the Tissue of Lymphogranuloma Benign, Acta. med. Scandinav. **106:** 239, 1941.
2. Longcope, W. T.: Sarcoidosis or Besnier Boeck-Schaumann Disease, J. A. M. A. **117:** 1321, 1941.
3. Hunter, F. T.: Hutchinson-Boeck's Disease, New England J. Med. **214:** 346, 1936.
4. Boeck, C.: Multiple Benign Sarcoid of Skin, J. Cutan. & Genito-Urin. Dis. **17:** 543, 1899.
5. Jungling, O.: Ueber ostitis tuberculosa multiplex cystoides, Beitr. z. klin. Chir. **143:** 401, 1928.
6. Longcope, W. T., and Pierson, J. W.: Boeck's Sarcoid, Bull. Johns Hopkins Hosp. **60:** 223, 1937.
7. Nickerson, S. A.: Boeck's Sarcoid: Report of Six Autopsied Cases, Arch. Path. **24:** 19, 1937.
8. Pinner, M.: Noncaseating Tuberculosis, Am. Rev. Tubere. **37:** 690, 1938.
9. Longcope, W. T., and Fisher, A. M.: Involvement of the Heart in Sarcoidosis, J. Mt. Sinai Hosp. **8:** 784, 1942.
10. Tillgren, J.: Diabetes Insipidus as a Symptom of Schaumann's Disease, Brit. J. Dermat. **47:** 223, 1935.
11. Rakov, H. L., and Taylor, J. S.: Sarcoidosis, J. Lab. & Clin. Med. **27:** 1284, 1942.
12. Lenartowicz, J., and Rothfeld, J.: Ein Fall von Hautsarkoiden mit identischen veränderungen im Gehirn und den inneren Organen, Arch. f. Dermat. u. Syph. **161:** 504, 1930.
13. Bernstein, M., Konzlemann, F. W., and Sidlick, D. M.: Boeck's Sarcoid; Report of a Case with Visceral Involvement, Arch. Int. Med. **44:** 721, 1929.
14. Palmer, W. L., Schindler, R., Templeton, R. E., and Humphreys, E. M.: Syphilis of The Stomach; Case Report, Ann. Int. Med. **18:** 393, 1943.
15. Williams, C., and Kimmelstiel, P.: Syphilis of the Stomach, J. A. M. A. **115:** 578, 1940.
16. Hebbel, R.: Chronic Gastritis: Its Relation to Gastric and Duodenal Ulcer and to Gastric Carcinoma, Am. J. Path. **19:** 43, 1943.

COMPOUND CRANIOCEREBRAL INJURIES

WILLIAM J. GERMAN, M.D., BERNARD S. BRODY, M.D., AND
SAMUEL C. HARVEY, M.D., NEW HAVEN, CONN.
(From the Department of Surgery, Yale University School of Medicine)

THE present shortage of specialists in many communities necessitates that the general surgeon again become a general surgeon in fact as well as in name. This applies to the field of neurosurgery, where a high percentage of those certified in this specialty are now serving with the Armed Forces. Within the Services, certain neurosurgical procedures must likewise be carried out by general surgeons, due to the necessary distribution of neurosurgeons over a vast geographical area. In both civilian and service practice the problems of trauma to the nervous system frequently require the attention of the general surgeon. Of these problems, compound craniocerebral injury is the subject which most often requires urgent, definitive, rational treatment. The present report is based upon the methods of treatment and the results obtained in patients with compound craniocerebral injuries admitted to the New Haven Hospital over a period of fourteen years.

Prior to World War I there was no unanimity of opinion concerning the treatment of compound craniocerebral wounds. During the early years of that war, operations for these wounds acquired bad repute from the high incidence of infection and death. Even scalp wounds were subject to frequent infection. Cushing's critical analysis of this situation was crystallized in his statement that the poor results were "largely due to delay—delay in transit, which may be avoidable; unnecessary delay after admission, which often is avoidable." In addition to his emphasis upon early treatment, Cushing[1] made an outstanding contribution by devising and applying methods of treatment in which "the same principles of débridement utilized so successfully for wounds elsewhere have in their essentials been adapted to wounds involving the brain." His results with débridement en bloc were presented in one of the finest surgical contributions that ever emerged from the smoke of battle.[1]

After World War I these principles were applied to the treatment of civilian injuries. In 1923 Harvey[2] reported on a group of 154 patients with skull fracture treated in the New Haven Hospital between 1919 and 1923. In this series the dura was penetrated in 14 patients (9 per cent); of these, 4 died, a mortality of 28 per cent. Of the 9 operated upon, 1

Presented in part at the meeting of the Society of University Surgeons, Nashville, Tenn., Feb. 10-12, 1944.
Received for publication, April 23, 1944.

TABLE I

HEAD INJURIES ACCORDING TO SEVERITY
(CUSHING, 1918)

	MORTALITY (%)
Scalp, intact cranium and dura	4.5
Local fracture, dura intact	9.2
Depressed fracture, dura punctured	11.8
Fracture, bone fragments in brain	24.0
Bone and projectile in brain	36.6
Penetrating ventricles, bone	42.8
Penetrating ventricles, projectile	100.0
Craniocerebral, air sinuses	73.0
Craniocerebral, traversing	80.0
Craniocerebral, with massive fracture	50.0

died on the table with a traversing wound and extensive intracranial hemorrhage. There were no deaths from infection. Harvey stated, "From experience gained during the late war it is known that wounds thoroughly débrided and sutured in the first six hours heal per primam in something over 90 per cent, while the delay of twelve hours adds not more than 10 per cent to the number that will break down. It takes, then, in most instances, from six to twelve hours for the infective agent to establish itself in the tissues in such a manner that it cannot be eradicated by thorough débridement."

Later, for reasons which are difficult to evaluate, there appeared in some localities a tendency to delay operative treatment. Munro,[3] in 1938, advocated a delay of twenty-four hours in all instances but advised against operation after forty-eight hours. In Munro's series of 136 operable injuries the mortality was 30.8 per cent, and the morbidity, chiefly due to infection, was stated to have been about 24 per cent, although all but 5.5 per cent were thought to be attributable to technical errors. In 1943 Munro[4] reported on study of 218 patients with compound fracture of the skull; 159 (73 per cent) were considered operable. The incidence of compound fractures of the skull in the entire group of patients with head injuries treated by Munro was 11.3 per cent. The operative mortality was 15.7 per cent. The incidence of infection in the patients operated on was 24.5 per cent. Munro considered as septic all wounds that did not heal by first intention; in case drains were inserted, the union of the wound, exclusive of the drainage tract, was used as the measure of the type of healing. In this series he eliminated the period of delay except in those cases in which the patient's condition was not satisfactory. Munro further advised that the operation be done before forty-eight hours after the receipt of the injury or else postponed for from six to eight months.

At the beginning of World War II the British[5] recognized the advisability of providing for early treatment of compound craniocerebral injuries by specially equipped and trained teams. Mobile neurosurgical units were utilized, but in France they were captured before their worth

had been tested. A similar attempt was made in the Middle East, but owing to the difficulty of segregating casualties in the forward areas, only 10 per cent of those reaching the neurosurgical unit had head injuries. It was therefore decided to base the unit behind the general hospital. This meant a delay in primary operation of approximately forty-eight hours. Working under these conditions, Ascroft[6] reported a series of 516 wounds (Table II) due to missiles; 292 were associated with penetration of the dura. The wounds received preliminary cleansing; sulfonamide powder was used and sulfadiazine was given by mouth or intravenously after operation. The mortality rate was excellent: 1.5 per cent in those with intact dura; 15 per cent with dural penetration. But a disquieting feature was that about 1 of 4 (75 out of 292) patients with penetrating wounds developed brain abscess. There were 17 deaths due to brain abscess. About 40 per cent of all deaths in Ascroft's series were due to abscess, and abscess played a part, often decisive, in rendering unfit for military service 40 per cent of all men incapacitated by penetrating wounds of the brain.

With the break-through at El Alamein, the lines of communication became so long that Eden,[7] who was then in charge, moved forward. His series of 293 patients (Table II) included 102 with compound cranial injuries with penetration of the dura and most of them were operated upon within twenty-four hours of injury, although in a few the wounds were more than three days old. Most of the patients reaching Eden had had no treatment other than a dressing of sulfanilamide powder to the wound and sulfanilamide orally or sulfadiazine intravenously. The incidence of intracranial infection in 102 patients with dural penetration was as follows: meningitis, 5; cerebral abscess, 1. As a result of getting patients with such wounds for early treatment the lowered incidence of infection is well reflected in the fall of serious complications as compared with Ascroft's results. The postoperative mortality in the 102 patients with dural penetration was 23.6 per cent (Eden). Primary healing of the wounds was obtained in over 90 per cent of the patients operated upon within the first forty-eight hours. Table II gives a compilation of Ascroft's and Eden's results.

TABLE II

COMPARATIVE MORTALITY FIGURES IN THE ASCROFT AND EDEN SERIES

	NUMBER OF PATIENTS		MORTALITY			
			ALL CAUSES (%)		FROM INFECTION (%)	
	ASCROFT	EDEN	ASCROFT	EDEN	ASCROFT	EDEN
Scalp wound	85	139	0	0	0	0
Fracture skull (dura intact)	139	69	1.5	1.4	0	0
Fracture skull (dura penetrated)	292	102	15.0	23.6	8.5	5.0
Total	516	310	9.0	8.6	4.8	1.6

Another striking example of the advantage of early operation is the report of Cloward[8] on a group of cranial injuries arising from the Pearl Harbor attack (he was not permitted to report the number of persons treated). Nearly all of the wounds were compound depressed fractures of the skull produced by fragments of shrapnel. His policy was to operate as soon as possible, but because of the large number of patients treated, it was necessary in many instances to delay as long as from twenty-four to thirty-six hours. No infection was encountered in any of the patients in whom a preliminary cleansing of the wound was carried out and sulfonamide powder used locally. It is unfortunate that Cloward's excellent results were attributed, by many, entirely to the effectiveness of sulfonamide therapy and the factor of early, skillful operation under favorable circumstances was overlooked.

The present series consists of 64 patients with compound craniocerebral injuries treated at the New Haven Hospital from 1928 to 1942. Basilar fractures through the air sinuses without exposure of the dura or brain were not included. Four patients died within one and one-half hours after admission to the hospital before preparations for operation were completed. The remaining 60 patients were operated upon. The operators included five members of the senior staff and the neurosurgical residents. The general policy in treatment was as follows: (1) immediate treatment of shock if present; (2) inspection and *not* palpation of the wound; (3) x-ray for extent of fracture, especially for depression and sinus involvement; (4) operation within six hours in *all* patients surviving the preparatory period (usually two hours). Local novocain was the anesthetic of choice. The essentials in the surgical procedure were (1) thorough débridement of the scalp, cranial wound, and devitalized brain tissue; (2) removal of indriven bone fragments and foreign bodies; (3) closure of the dura (silk) if possible; (4) closure of the scalp in two layers (silk); (5) drainage of the frontal sinuses and of most wounds for culture. The bone removal was usually en bloc for the comminuted and depressed fractures, unless the frontal or sagittal sinuses were involved, in which case fragments were removed. In the case of linear fractures, the fissures were cleaned, but no bone was removed.

The distribution of patients according to age is shown in Table III. About 60 per cent of the patients were in the first three decades, but a significant number (14 per cent) were over 60 years of age. It is noteworthy that all of these patients in the seventh and eighth decades died;

TABLE III

DISTRIBUTION AS TO AGE (64 CASES)

	DECADE							
	1	2	3	4	5	6	7	8
Number of cases	11	11	16	7	7	3	7	2
Deaths	3	1	1	2	0	1	7	2

53 per cent of the total mortality (9 of the 17 deaths) occurred in this group.

The sex incidence followed roughly a ratio of 4 to 1 in favor of the males. The injury was due to a missile in 9 patients. The remaining 55 were injured as follows: Automobile accident, 42; accidental fall, 5; struck by blunt object, 8.

Associated injuries were present in 33 patients, being minor in 11 and major in 22. Fractures of the facial bones, ribs, and long bones accounted for 19 of the major injuries; laceration of the liver was noted in 1. The minor injuries consisted of contusions and lacerations.

Period of Unconsciousness.—There were 15 patients who gave no history of loss of consciousness, although it is possible that in some of these at least a transient break in the stream of consciousness may have escaped recognition. Twenty-three patients were semiconscious or unconscious for less than one hour, 18 from one to ten hours, and 8 for more than twenty-four hours. Thirteen patients died without regaining consciousness. Coma is generally recognized as a grave prognostic sign. Table IV shows the postoperative mortality classified in terms of the degree of consciousness on arrival at the hospital.

TABLE IV

MORTALITY RELATED TO STATE OF CONSCIOUSNESS

	COMA	SEMICONSCIOUS	ALERT
Number dying	16	0	1*
Number surviving	9	7	31

*See text.

The single fatality in the alert group* was a patient 65 years of age who died of a cerebral hemorrhage on the third day following the injury (bullet). One patient in coma on arrival died of a complicating infection. It is notable that more than one-third of the patients arriving in deep coma survived. It does not seem warranted therefore to leave these patients for some hours the better to assess their chances while at the same time increasing the possibilities of infection by delay. However, where large numbers of battle casualties require urgent treatment, the state of consciousness is an important factor in selecting the more favorable cases for early operation (Eden[7]).

Shock.—The records were adequate for the determination of the presence of shock in 59 of the 64 patients. On the basis of a systolic blood pressure below 100 on admission or at the beginning of the operation, shock was present in 15. Seven of these patients died; of these, 2 died before preparations for operation had been completed. An analysis of the remaining 5 deaths shows the time and cause as follows: (1) Four and one-half hours, extensive brain damage and compound fractures of

*See Table IV.

both legs (operation consisted only of closure of scalp wound); (2) six hours, gross laceration of brain with brain tissue extruding; (3) twenty-four hours, extensive subdural hematoma found at post-mortem; (4) seven days, bilateral bronchopneumonia; (5) five weeks, intracranial infection. Four of these patients were over 60 years of age. Moderate shock was present at the beginning of the operation in only 4 of the 60 patients. Shock should rarely delay an operation for more than six hours. With present methods for the treatment of shock it should be possible to correct this condition within six hours except in those with the most severe intracranial injuries and in those with continuous concealed hemorrhage in the abdomen or thorax.

Operations.—Four patients died within one and one-half hours after the injury, before preparations for operation were completed. The remaining 60 patients were taken to the operating room as soon as the extent of the injury was determined and appropriate measures for the treatment of shock and associated injuries were completed; the operability rate was 93.8 per cent. Operation was begun within six hours after the injury in all but 2 patients.

TABLE V

TIME INTERVAL BETWEEN INJURY AND OPERATION

Number of hours	Less than 4	4 to 6	7	9
Number of cases	48	10	1	1

Types of Operations.—Bloc removal of the compound scalp and cranial wound was done in 19 of the 52 patients in whom projectiles were not involved. This group included most of the more severely injured. The operative mortality was 26 per cent. Excision of the scalp wound and fragment removal of the cranial wound was done in 20 patients, including those with orbitonasal injuries and many with less severe injuries to the cranial vault. The operative mortality was 10 per cent. Débridement of the scalp wound without bone removal was done in 13 patients. The wounds were chiefly linear fractures with little or no depression. The operative mortality was 7.7 per cent. The total operative mortality for the entire series of 52 patients with nonprojectile injuries was 15.4 per cent. The series of projectile injuries (9) was too small to assess the results in relation to the types of operative procedure employed.

Primary closure of the scalp wound was done in all instances. Drains were inserted in the wounds of 29 of the 60 patients operated on; the drains were usually removed within twenty-four or forty-eight hours. The dura was closed whenever possible; the reasons for leaving the dura open were as follows: pinpoint openings, dural tension, and shredded dura.

Postoperative Infection.—Records of patients who died in the first six days following operation were not included in the statistical analysis

(Table VI), since the time interval was not sufficient to exclude the possibility of infection had the patient survived. In the remaining 51 patients, serious infection was present in 2, and of these, 1 died, a mortality of 2 per cent. Infections confined to the drainage tracts were included as wound infections.

TABLE VI

POSTOPERATIVE INFECTION (51 PATIENTS LIVING OVER SIX DAYS)

Cerebritis	1	(2%)
Meningitis	1	(2%)
Local osteo.	2*	(4%)
Scalp	7	(14%)
Total	10	(20%)

*Local osteo. and meningitis in one patient, with nasofrontal injury.

Only 2 scalp infections occurred in patients in whom drainage had not been used. A complete bloc débridement was done in only 1 of the patients developing infections. The débridement in these patients was limited in most instances because the frontal sinus was close to or involved in the fracture.

Munro[9] reported a bacteriologic study of 70 patients with compound fractures of the skull. It appears that the degree of culturable contamination of the wound varies from 55 to 60 per cent during the first forty-eight hours and rises sharply thereafter. Thirty-one wounds were swabbed within twenty-four hours or less of the receipt of the injury. Seventeen (55 per cent) of this group showed pathogenic bacteria (*Staphylococcus aureus* in all but two). Forty-four wounds were forty-eight hours old or less when cultured. Twenty-six grew pathogenic bacteria (pure *Staph. aureus* in 21 of these). The rather high incidence of contaminated wounds within the first twenty-four hours with pathogenic organisms underscores the necessity for early and thorough débridement. Many of the staphylococcal wound infections are endogenous and not exogenous in origin, yet care must be taken *not to introduce contamination* into the wound by unnecessary finger palpation. Brain wounds in battle casualties are seldom sterile. The Russians found only 2 of 300 such wounds to be sterile.

Mortality.—It has been said by many writers that mortality figures have little real significance since no two studies are based upon identical clinical material. Eden[7] stated, "The mortality figure has really little meaning, for the mortality in these cases depends to a great extent on how near you are to the front and what you operate on." In the present series, no patient was denied operation because he was considered to be a "poor risk." The operability rate of 93.8 per cent included all patients who survived for over one and one-half hours following injury. The *total mortality* in the entire series of 64 patients was 26.5 per cent, only a trifle higher than Munro's[3] estimate of 24 per cent for the aver-

age mortality of about 120,000 cases of all types of head injuries, most of which were of the closed type. The *operative mortality* in all compound craniocerebral injuries in the present series was 21.6 per cent.

Of the 9 patients in this series with injuries due to missiles, 6 died (1 before operation), a mortality of 66.7 per cent; operative mortality, 62.5 per cent. All 4 of the patients with traversing wounds died following operation. The single fatality resulting from nontraversing missiles (mortality 25 per cent) was due to severe kidney damage and uremia from prophylactic sulfapyridine therapy.

There were 52 patients operated upon for injuries not produced by projectiles, with a *mortality* of 15.4 per cent. One-half of the postoperative deaths occurred in patients over 60 years of age.

TABLES VII

OPERATIVE MORTALITY RELATED TO SEVERITY OF INJURY
(52 CASES OF COMPOUND FRACTURE—EXCLUSIVE OF INJURIES DUE TO MISSILES)

	CASES	DEATHS
I. Fracture, dura intact	29	2 (7%)
II. Fracture, dura open	6	1 (17%)
III. Fracture, dura open plus laceration or contusion of brain	9	2 (22%)
IV. III plus indriven bone fragments	8	3 (37%)
Total	52	8 (15.4%)

Cause of Death.—Autopsies were obtained in 5 of the 17 patients who died. All 5 of these patients had been operated upon. Four patients died before operation. The projectile injuries account for 35.3 per cent of the total deaths.

TABLE VIII

CAUSE OF DEATH—PROJECTILE INJURIES
(9 CASES, 6 DEATHS)

Extensive brain damage	3*
Massive subdural hemorrhage	1
Renal hemorrhage, uremia, prophylactic sulfapyridine	1
Cerebral hemorrhage, hypertension	1
Total	6

Deaths in missile group (3 over age of 60).
*No operation in one.

TABLE IX

CAUSE OF DEATH—NONPROJECTILE INJURIES
(55 CASES, 11 DEATHS)

Extensive brain damage	7*
Contralateral subdural hematoma	1
Infection (cerebritis)	1
Bronchopneumonia	2
Total	11

Deaths in group with nonprojectile injuries (6 over age 60).
*No operation in three.

Summary and Conclusions.—Accumulated experience during World War I indicated that early operation and thorough débridement were of primary importance in the treatment of compound craniocerebral injuries. Cushing was largely responsible for laying down these principles of treatment as an essential basis for controlling infection, which was so largely responsible for the high mortality encountered in the early years of World War I. Later, for reasons difficult to evaluate, there appeared in some localities a tendency to delay operative treatment. At the beginning of World War II the British policy included early treatment of compound craniocerebral injuries, and a comparative study of two series (Ascroft, Eden) indicates a higher incidence of serious infection where operation was unavoidably delayed.

The present report consists of 64 compound craniocerebral injuries treated at the New Haven Hospital from 1928 to 1942, 9 of which were due to missiles. Sixty patients were operated upon; 4 patients died within one and one-half hours after admission to the hospital. No patient was denied operation because he was considered to be a "poor risk." It is notable that more than one-third of the patients arriving in deep coma survived. It does not seem warranted therefore to leave these patients for some hours the better to assess their chances while at the same time increasing the possibility of infection by delay. Operation was begun within six hours in all but 2 patients. Moderate shock was present at the beginning of the operation in only 4. With present methods for the treatment of shock, it should be possible to correct this condition within six hours except in the most severe intracranial injuries and in those patients with continuous bleeding in the abdomen or thorax.

The general policy in treatment was as follows: (1) immediate treatment of shock *if present;* (2) inspection and *not* palpation of the wound; (3) x-ray for extent of fracture, especially for depression and sinus involvement; (4) operation within six hours in *all* patients surviving the preparatory period (usually two hours). Thorough débridement of the scalp, cranial wound, and devitalized brain tissue was stressed. The bone removal was usually en bloc for the comminuted and depressed fractures, unless the frontal or sagittal sinuses were involved, in which instance fragments were removed. Complete excision of the scalp and brain wounds and removal of foreign bodies from the brain were considered essential in averting infection. Serious infection occurred in only 2 patients in this series, 1 of whom died; the mortality from infection was 2 per cent.

The *total mortality* for the entire series of 64 cases was 26.5 per cent, only a trifle higher than Munro's estimate of 24 per cent for the average mortality of about 120,000 cases of all types of head injuries, most of which were of the closed type. The projectile injuries (9 cases) accounted for 35.3 per cent of the total deaths. The *operative mortality* of all compound craniocerebral injuries in this series was 21.6 per cent.

There were 52 patients operated upon for injuries not produced by projectiles, with an *operative mortality* of 15.4 per cent. One-half of the postoperative deaths occurred in patients over 60 years of age.

REFERENCES

1. Cushing, H.: A Study of a Series of Wounds Involving the Brain and Its Enveloping Structures, Brit. J. Surg. **5**: 558-684, 1918.
2. Harvey, S. C.: Compound Cranio-Cerebral Injuries, Boston, M. & S. J. **189**: 911-914, 1923.
3. Munro, D.: Cranio-Cerebral Injuries: Their Diagnosis and Treatment, London, New York, 1938, Oxford University Press.
4. Munro, D.: Compound Fractures of the Skull. The Results of Surgical Therapy in Two Hundred and Eighteen Cases, New England J. Med. **228**: 737-745, 1943.
5. Cairns, H., and Guttmann, E.: A Review of Recent German Work on Gunshot Wounds of the Head, Bull. War Med. **3**: 477-484, 1943.
6. Ascroft, P. B.: Treatment of Head Wounds Due to Missiles. Analysis of 500 Cases, Lancet **2**: 211-218, 1943.
7. Eden, Kenneth: Mobile Neurosurgery in Warfare, Lancet 2: 689-692, 1943.
8. Cloward, R. B.: War Injuries to the Head. Treatment of Penetrating Wounds, J. A. M. A. **118**: 267-270, 1942.
9. Munro, D.: The Bacteriology of the Wounds of Compound Fractures of the Skull, New England J. Med. **227**: 939-944, 1942.

IMPROVED RETRACTOR FOR HEMILAMINECTOMY*

LIEUTENANT C. HUNTER SHELDEN, AND LIEUTENANT ROBERT H. PUDENZ
MEDICAL CORPS, U. S. N. R.

ADEQUATE exposure in the limited operative field is essential for successful removal of protruded intervertebral discs. The average laminectomy retractor was designed to retract both sacrospinalis muscle groups, thus allowing complete removal of the spinous processes and laminae. Hemilaminectomy requires the separation of only one muscle group from the spinous process. This more conservative procedure introduces a new problem of exposure because the mesial margin of the operative field includes the bony spinous process. Fixation of one blade of the usual retractor to the bone is not only difficult but, if successful, occupies valuable space in the already limited field of exposure. If the mesial blade is inserted into the fascia and muscle of the opposite sacrospinalis muscle group, the situation is somewhat improved but still not ideal because the blade in the wound must be placed at a deeper level. Thus, with strong retraction it is difficult

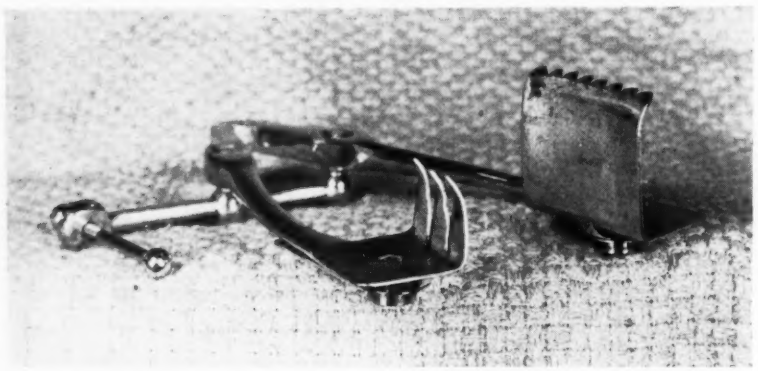


Fig. 1.—Photograph of retractor showing shape of the blades.

to prevent the deeper of the two blades from slipping. This allows the muscle fibers adjacent to the lamina to slide from beneath the retractor. If the blade against the muscle is deep enough to catch all the muscle fibers, there is frequently a rotation of the entire retractor because of the extreme difference in depth of the two blades.

In an attempt to obviate these mechanical difficulties a retractor was designed with blades of unequal length (Fig. 1). The shorter blade has three long teeth which are inserted through the lumbar fascia

*The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or as reflecting the views of the Navy Department or the Naval Service at large.

Received for publication, May 29, 1944.

adjacent to the spinous processes. The longer blade, which is used for the muscle retraction, is two inches wide, slightly curved, and has small laterally bent serrations on the free end which fix the blade at the desired depth. The ease with which these blades may be produced in any machine shop makes it possible to have several lengths available.

These blades are attached to the arms of a Lilienthal rib spreader which possesses a screw adjustment that allows forceful retraction. The Lilienthal retractor was selected because it possesses removable

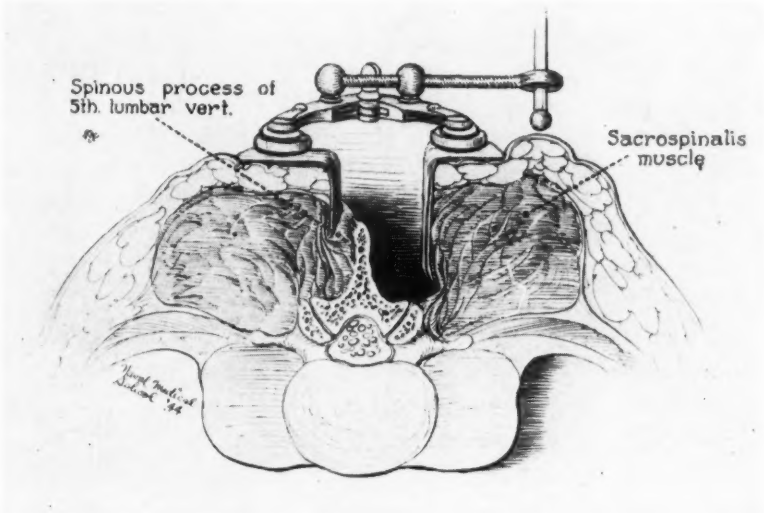


Fig. 2.—Exposure for hemilaminectomy, demonstrating method of muscle retraction.

blades, a distinct advantage when converted into a laminectomy retractor for it allows one to use a blade which corresponds in length to the size of the sacrospinalis muscle group. The exchange of blades is a simple matter and requires but a few seconds.

Hemilaminectomy is simplified and exposure improved particularly in those individuals with strong muscles and poor relaxation (Fig. 2). Although originally designed for lumbar hemilaminectomy, it has proved to be equally adapted for use in the cervical region.

A LIMITED COMPARISON OF CONTINUOUS SPINAL AND GENERAL ETHER ANESTHESIA

WILLIAM GRANT COOPER, II, M.D., WILMA ZUMWALT, R.N., AND EVERETT D. SUGARBAKER, M.D., COLUMBIA, MO.

(From the Surgical Department of the Ellis Fischel State Cancer Hospital)

THE relative advantages of spinal and inhalation ether anesthesia have been the subject of much discussion. The primary weakness of spinal anesthesia as heretofore administered, and the one on which many of the objections to its use have depended, has been the uncertainty of and the inability to lengthen its duration. This shortcoming may now be completely eliminated by the use of the continuous principle, so that it seems worth while to attempt a revaluation of the subject. An exceptional opportunity to do this was presented when a particular series of anesthetics were given at this hospital. From January, 1940, to February, 1942, one of us (W. Z.) gave all the general ether anesthesias, and from February, 1942, to September, 1943, gave continuous spinal anesthesia to all patients requiring operation below the diaphragm.

The patients' age groups, their general condition, the primary diagnosis, and procedures carried out under each type of anesthesia were essentially similar. The operations were done by or under the supervision of only two surgeons.

The general anesthetics were administered by the closed system. Nitrous oxide was used for induction and the anesthesia maintained with inhalation ether and oxygen. This method has traditionally been satisfactory. The continuous spinal anesthetics were given by the method of Lemmon with certain modifications, which will be discussed later. No attempt was made to select cases for spinal anesthesia. That is to say, no patient was denied spinal anesthesia because something about his condition raised theoretical objections to its use.

This hospital treats indigent patients suffering from cancer. The average age on admission is about 60 years, and anemia, hypoproteinemia, and the diseases associated with advanced age are commonly seen in association with the tumor for which treatment is sought. Poor general condition is particularly frequent in those subjected to abdominal operation, as most of these are patients with gastrointestinal cancer. Careful attempt is made preoperatively to restore these patients physiologically as nearly as possible to normal. Still they present a severe test of the efficiency and safety of whatever anesthetic method is used.

Received for publication, April 6, 1944.

The material selected for study consists of two series of 100 anesthetics each. The first group comprises the last consecutive 100 general anesthetics given for operations below the diaphragm. The second group consists of the first and the last consecutive 50 continuous spinal anesthetics given by the same anesthetist. As continuous spinal anesthesia is used only for operations below the diaphragm, the two groups are nicely comparable. The first and last 50 cases in which the patients were given continuous spinal anesthesia were considered in order to compare results obtained earlier with those obtained after we had acquired some experience with this method.

The comparative tabulation is presented in Table I.

TABLE I

INDICATING THE SIMILARITY OF THE TWO GROUPS

	CONTINUOUS SPINAL ANESTHESIA	GENERAL ANESTHESIA
Average age (yr.)	60	55
Per cent with cancer	72	69
Radical intestinal resections	20	21
Other extensive majors	7	8
Inoperable exploratory laparotomies	22	18
Remaining number of cases	51	53
Cases requiring over two hours	50	37
Cases requiring under two hours	50	63
Average crystalloids given in operating room	900 c.c.	400 c.c.
Average amount of blood given in operating room	300 c.c.	300 c.c.

In Table I it may be noted that the average age of the patients in each group is approximately the same. The percentage of the patients suffering from cancer is given, as this is an extremely important factor in the preoperative condition. Of the patients in the group having radical intestinal resections or other extensive major procedures the number of patients receiving each anesthetic is approximately the same. The "exploratory" cases include those patients in whom an exploratory abdominal operation revealed an inoperable condition, and cecostomy, gastrostomy, or only biopsy was done. Although these latter are not extensive procedures, they carry the gravest immediate prognosis because of the uniformly poor condition of such patients. The slightly greater length of time required for operations done under continuous spinal anesthesia is probably due to the fact that the surgeon felt less hurried by the condition of the patient. It is noted that more fluid was given intravenously in the operating room to the patients receiving continuous spinal anesthesia than to those receiving ether anesthesia. The explanation of this is that the administration is begun at the start of the operation in continuous spinal anesthesia and the blood given in these patients was preserved with an equal amount of dextrose-buffer-citrate solution. Previously, it had been given as citrated whole blood.

TABLE II

COMPARISON OF OPERATIVE AND POSTOPERATIVE COURSE (200 CASES)

	CONTINUOUS SPINAL ANESTHESIA	GENERAL ANESTHESIA
Satisfactory anesthetic and postanesthetic course	77	44
Satisfactory anesthesia with unrelated deaths (late)	2	3
Satisfactory anesthesia with postanesthetic disorientation	2	1
Satisfactory anesthesia with hypotension in operating room or postoperatively	10	34
Operative shock	2	10
Fatal shock	2	2
Postoperative atelectasis	1	1
Fatal bronchopneumonia (within three days postoperatively)	2	2
Fatal emboli	0	3
Severe postoperative headache	1	0

In Table II, evaluating the anesthetic and the postanesthetic course, a patient's condition was considered satisfactory if the vital signs remained unchanged throughout the time on the operating table and for twelve hours postoperatively and if no technical or anesthetic complications occurred.

Two patients receiving continuous spinal anesthesia and three patients receiving ether died after a gradual downhill course. All these deaths were in patients suffering from abdominal carcinomatosis demonstrated at operation, and their deaths are in no way referable to the anesthetic as such. Three patients became disoriented postoperatively, but all three were in subclinical uremia. This was felt to be the cause of their disorientation rather than the anesthetic. All three recovered.

Hypotension was defined for our purposes as a blood pressure fall in the operating room or within the first twelve hours postoperatively to a systolic level below 90 mm. mercury pressure, or a fall of more than one-third the systolic pressure in patients whose preoperative reading was over 150 systolic. This hypotension was not accompanied by pulse variation of great degree, nor in any instance did it last over ten minutes. It responded promptly to the administration of intravenous ephedrine or saline solution in the patients given continuous spinal anesthesia and to the administration of appropriate stimulants in those given general anesthetics. Patients who did not respond to these therapeutic measures but required transfusions were not considered to be suffering from hypotension but from shock and the results are listed separately.

In comparing the first 50 and the second 50 cases in which the patients were given continuous spinal anesthesia, it is found that eight of the ten episodes of hypotension occurred in the first 50 patients, and we feel that the case records in the latter group show a smoother and more nearly perfect anesthetic course and postoperative recovery.

In those previously considered groups we have the totals of 92 satisfactory continuous spinal and 81 satisfactory general anesthetics, which leads to the remainder of the patients in the series in whom complications were encountered.

Shock occurred in twelve patients. In those receiving continuous spinal anesthesia there were only two instances. Both occurred during bowel resection. In those given ether five occurred in bowel resection and five in massive major cases. The difference in favor of the continuous spinal anesthesia is probably due, in considerable part, to the security felt with this anesthetic in suspending all manipulation as soon as any blood pressure drop was reported until the vital signs had returned to normal. Review of the case records also gives the impression that in the patients given ether there was occasional hesitancy or

Fig. 1.—Continuous spinal anesthesia setup. Only special features are malleable spinal needle (*A*), fine bore rubber tubing (*B*), and thick mattress with space cut out to accommodate needle (*C*). Insert shows simple means of eliminating annoying stopcock by replacing with short length (1¼ inch) of gum tubing and clamp.

delay in giving blood, although the total amount given was usually the same. The patients were not given transfusions at the first suspicion of shock, some time occasionally elapsing before blood was started. A readily available source of this fluid, such as is provided by a blood bank, now obviates this difficulty. The routine preoperative cross-grouping of the patients with blood available in a bank and the placing of a cannula in a vein at the beginning of every operation allows greater ease and speed in the giving of a transfusion. In all fairness we feel that this prophylactic administration of blood is a

factor also partly responsible for the decreased number of cases of shock in the patients given continuous spinal anesthesia.

Four patients died in circulatory collapse, either during or shortly after the operative procedure. Two were in each group. Three of these patients had large bowel resections and one had a hemipelvectomy. In all instances the operative trauma and the poor preoperative

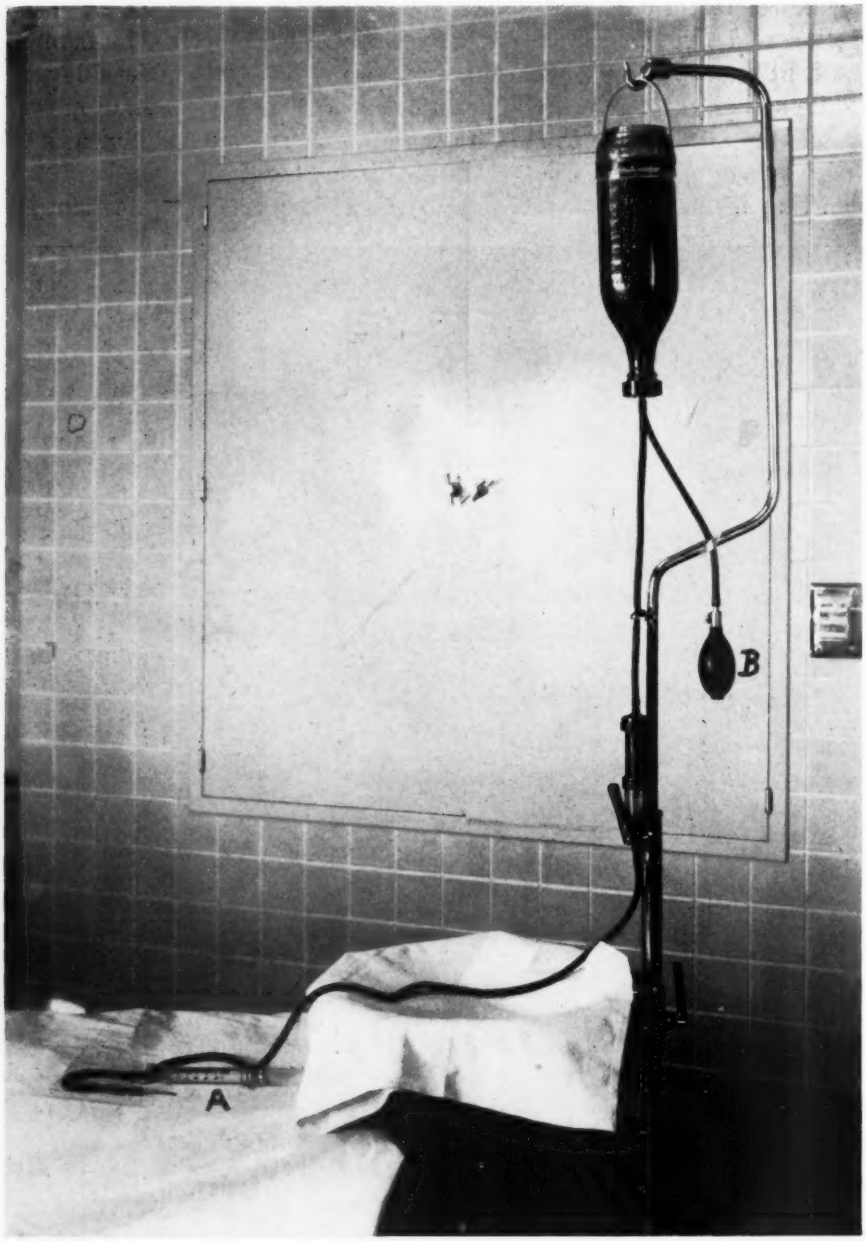


Fig. 2.—Intravenous apparatus which is always set up before continuous spinal anesthesia is begun in any major operation. *(A)* Syringe in circuit for administration of ephedrine and pentothal; *(B)* rubber bulb to provide for more rapid administration of blood or plasma as an occasion may demand.

condition of the patient was sufficient to explain the fatality without implication of the anesthetic used.

The pulmonary complications were equal in each group and the incidence is not unduly high in either. The two patients developing clinical atelectasis had uneventful recoveries. The patients dying early of bronchopneumonia were all in the exploratory laparotomy group and were extremely poor operative risks. It is interesting that fatal emboli (proved at post-mortem examination) occurred in three patients given ether, whereas, none have so far been encountered in any of the patients given continuous spinal anesthetics (300) to date.

As to the complications peculiar to those given continuous spinal anesthesia, the patient who developed headache suffered severely from it for two weeks postoperatively with complete recovery. He also had headaches from a single dose of spinal anesthesia and would now be considered an unsuitable candidate for this method. In another patient (case not tabulated) the anesthetic solution leaked around the needle but good relaxation and loss of sensation was obtained. No difficulty followed except that an excessive amount of procaine had to be used.

The method by which continuous spinal anesthesia has been administered in these 100 patients and in the other 200 patients to whom we have given it is as follows:

In the operating room the apparatus and technique suggested by Lemmon,[1] with certain modifications to be discussed later, was used. Five per cent procaine was the anesthetic solution which we employed. Three and five-tenths per cent solution was tried previously and found inadequate as it did not produce a dependable level of anesthesia. Adjunctive sedation (not anesthesia) was secured with the intravenous administration of a 2.5 per cent solution of pentothal sodium. The anoxia present in old patients in poor condition under spinal anesthesia was combated by the administration of supplementary oxygen, 5 liters per minute. Intravenous administration of saline solution, blood transfusion, or plasma was used routinely to replace lost fluid.

The apparatus for continuous spinal anesthesia consists of a malleable No. 19 needle with a stylet. To this, a length of firm narrow lumen tubing is connected by an adaptor. The other end of the tubing is attached to a 10 c.c. syringe. A short (approximately 2 cm) piece of ordinary rubber tubing interposed between the syringe and the narrow tubing is used instead of a stopcock. A hemostat clamped across this controls flow of the anesthetic solution. When this large-guage rubber tubing is worn out, it can be easily and cheaply replaced, and it never sticks or gets out of order as is often the case with the smaller metal valves. The introducer for the malleable needle is seldom used because leakage of spinal fluid seemed to occur around the needle tract when it had been used for skin puncture on thin or small patients; and if the director is incorrectly placed at the first attempt, readjust-

ment is traumatic and occasionally difficult. An ordinary stab blade to puncture the skin usually suffices and the malleable needle is then inserted without further aid.

The patient is placed in a lateral recumbent position on a mattress,* which has a space under the lumbar region where the needle may later fit. The malleable needle is placed in the spinal canal in the third lumbar space for low abdominal procedures and in the second lumbar space for higher ones. The unsparing use of local 1 per cent procaine almost completely removes the discomforts of the puncture. Ten cubic centimeters of spinal fluid are removed and mixed with 500 mg. procaine. If more anesthetic solution is needed for longer procedures, normal saline solution is used as a diluent. Either solution works well. The syringe is connected to the tubing and then to the spinal needle, which has previously been placed in the spinal canal, after the air has been evacuated from the system. When, by testing, absolute free flow is assured, the patient is returned to the supine position with the neck acutely flexed. No anesthetic solution is given.

Under local anesthesia, a cannula is placed in a vein, preferably one in the ankle, and administration of intravenous saline solution begun. A catheter placed in the urinary bladder (this may be best done after anesthesia has been produced) and attached to a drainage bottle is used in all low abdominal procedures and in those upper abdominal procedures which may be long. The stomach tube, which is routinely inserted on the ward in patients in whom gastrointestinal surgery is planned, is opened and its free end allowed to drain into an emesis basin. A small intranasal catheter or mask is prepared for oxygen administration. The intranasal catheter is used when suction on the stomach tube may be necessary; otherwise, the mask is preferred. The vital signs are checked and the presence of free flow in the anesthetic solution system is confirmed. This is important because moving the patient may have affected the position of the needle, and adequate anesthesia is occasionally not obtained in the absence of absolute free flow. Ephedrine, 0.024 Gm., is injected into the intravenous tubing just before the procaine is to be administered. This routine and time of administration have, in our hands, proved to be the most satisfactory.

Now, 3 c.c. of the 5 per cent solution of procaine (150 mg.) are injected into the spinal canal. The patient is placed in 10-degree Trendelenberg position with the neck still acutely flexed and the desired level of anesthesia secured. At least 3 c.c. of procaine should be given if anesthesia to the nipple line is desired. The level of anesthesia rises slowly after the injection. Its progress is tested by following the gradual loss of response to pinpricks. When the desired extent of anesthesia is secured, usually within five minutes, the patient is returned to the level position. It is our clinical impression that this rise

*Such as that manufactured by George P. Pilling & Son Co., Philadelphia, Pa.

of anesthesia may be slower in patients with abdominal distention. Once the zone has been established, it will remain stationary, even if the patient is put in extreme Trendelenberg position and more procaine injected. Lesser amounts of anesthetic solution than 3 c.c. for the initial dose do not seem to secure adequate anesthesia to the nipple line, and supplementary doses merely maintain, but do not raise, the level. This height of anesthesia is adequate for all abdominal procedures. Operations on the lower abdomen and the extremities do not, of course, require it. Even with anesthesia as high as the nipple line, the patients will become apprehensive or complain of discomfort when a hand is placed between the liver and the diaphragm. This discomfort is transitory and largely eliminated by the use of pentothal sodium intravenously. The pentothal sodium is introduced in a 2.5 per cent solution in normal saline into the intravenous tubing as needed for hypnosis during long operation. Judiciously used it relieves completely the discomfort attendant upon upper abdominal exploration and the ennui of a long interval of time which the patient must spend restrained and in one position. Yet reliance is not placed on the pentothal for anesthesia; its only use is as a control of sedation. Intermittent injection of 1 c.c. of procaine every twenty or thirty minutes (with some variations, dependent upon the procedure, age, size, and condition of the patient) will maintain the anesthesia. Five liters of oxygen per minute are administered through a mask or intranasal tube, because these patients have a diminished capacity for oxygen utilization due to emphysematous changes of age and the paralysis of the abdominal muscles of respiration. As soon as the anesthetic has reached the desired level, appropriate skin preparation and drape is performed and the operation may proceed.

The availability of pentothal sodium for intravenous administration relieves any concomitant discomfort which may go with the length of the procedure. The administration of oxygen intranasally prevents anoxia which might otherwise occur. In long operative procedures the patients have secreted from 300 to 700 c.c. of urine, which is carried off by the urinary catheter. The stomach tube is helpful in decompressing the stomach when air swallowing has occurred. As part of the routine preoperative preparation, each patient is cross-grouped and blood is available in the hospital bank. With an intravenous cannula in place in an ankle vein and saline solution slowly running, a transfusion may be started if desired within two or three minutes of the time such a decision is made. All these details are extremely important, and each is necessary in contributing to the sum total of operating room control which can be available.

Ephedrine, 0.024 Gm., is given intravenously as needed to combat the fall in blood pressure due to the procaine, but only that due to the procaine. After the initial dose additional doses of like amount will probably be needed with each subsequent administration of 50 mg. of

novocain. Should either the anesthetist or the surgeon suspect that the present or next contemplated surgical maneuver will initiate shock, a blood transfusion must be started at once. Giving blood in anticipation of shock saves more lives than all therapeutic measures possible after collapse has become manifest. The differentiation of hypotension due to surgical shock and that due to procaine may be difficult at times but is usually evident from the facts at hand. If the blood pressure does not respond at once to 0.024 Gm. of ephedrine intravenously, the fall must be attributed to surgical shock and be so treated.

Postoperatively the employment of carbon dioxide inhalation, routine transfusions, low Fowler's position as indicated, and watchful care must be assured the patient as in general anesthesia. The details of this need not be elaborated here.

DISCUSSION

The introduction of the continuous principle into spinal anesthesia has made it possible to continue operations under spinal block for previously unheard of lengths of time. In a sense this has meant redevelopment of much of the technique of spinal anesthesia. Some of the factors requiring more attention as the result of the increased length of anesthesia were adequate oxygenation and aeration of the patient, control of blood pressure drops, and elimination of discomfort for these long periods. All of the cases presented here in which the patients received continuous spinal anesthesia were observed during this period of development which, to a more limited degree, is still continuing.

Resultant improvement in the management of the patients given spinal anesthesia is reflected in a limited comparison between the first and last 50 cases presented. All of the general anesthetics given were based on long experience with this method, so that it seems likely that the superiority of continuous spinal anesthesia is apt to become still more apparent than is indicated by this presentation as our acquaintance with it grows. We believe that the excellence of continuous spinal anesthesia is due primarily to three factors:

First, relaxation is sustained and complete, necessitating considerably less operative trauma. This is attested to by the fact that no fatal emboli occurred in the patients given spinal anesthesia as compared to three in those given ether anesthesia. Moreover, during unforeseen accidents, such as hemorrhage or gross spillage, maintenance of exposure and protective packs can be depended on.

Second, the surgeon is never hurried. Extensive and lengthy procedures are, unfortunately, most often necessary in patients whose general condition is least able to withstand them. On such occasions it is extremely gratifying to the surgeon to be able to take time for careful thought and meticulous work without regard to the duration of anesthesia. If surgical trauma becomes excessive and the blood

pressure drops, it has become our custom to suspend work immediately while blood or plasma is administered more rapidly and the patient is given ample opportunity to recover.

Finally, continuous spinal anesthesia is particularly advantageous in patients with cancer because it inherently provides for the element of uncertainty in all exploratory procedures where the operability must remain in question until the peritoneum has been opened. In the inoperable patient the small initial dose shortly wears off, returning the patient, with the exception of the incision, to his original preoperative state. In the operable case, provision is made for continuing unhurriedly as long as is necessary regardless of unforeseen difficulties.

SUMMARY

1. The results in 100 consecutive patients receiving general ether anesthesia and in 100 consecutive patients receiving continuous spinal anesthesia have been comparatively presented. It is felt that the relative constancy of all factors, with the exception of the type of anesthetic used, makes these unusually good groups for comparison.

2. On critical analysis, 44 per cent of the patients given general anesthesia and 77 per cent of those given continuous spinal anesthesia were considered to have had satisfactory operative and postoperative courses. The incidence of blood pressure falls was very appreciably less in those who received spinal anesthesia, with definite improvement in technique reflected in the course of the first and last fifty patients so treated. The occurrence of three fatal pulmonary emboli following the use of general ether anesthesia and none following the use of continuous spinal anesthesia, in our opinion, reflects the less complete relaxation produced by the former, necessitating greater operative trauma.

3. Our method of administration of continuous spinal anesthesia is similar to that described by Lemmon, with certain simplifying modifications. The management of these patients, involving considerably more than the periodic administration of a spinal anesthetic agent, is discussed from several of its important aspects.

CYSTOMETRY AFTER SPINAL ANESTHESIA

MAJOR CARROLL J. BELLIS, MEDICAL CORPS RES., U. S. ARMY

INTRODUCTION

CREEVY'S classical studies of the effects of prolonged vesical distention demonstrated that profound irreversible urinary tract damage may follow the neglect of the overdistended bladder. In the presence of urinary retention, there is an increased susceptibility of the urinary tract to infection; in fact, patients who were thought to have succumbed to obscure vasomotor effects following rapid decompression of the chronically distended bladder or to the infection attending catheterization really have died as a result of latent upper urinary tract infection harbored prior to the emptying procedure.[20]

Every cystoscopist is familiar with the mural hemorrhages in the acutely or chronically distended bladder (Mercier,[50] Grellety,[34] Picard,[56] Tuffier,[74] Genouville and Boeckel,[29] Delbet,[27] Chute,[18] and Vintici and Laroche[76]). Creevy[21] and others (Shigematsu,[70] and Guyon and Albarran[36]) have demonstrated these hemorrhages within forty-eight hours, by which time the postural tone (a protective mechanism) has failed, gangrene and perforation intervening in sixty to seventy-two hours. The hemorrhages occur first in the submucosa of the bladder, then occupy the entire wall and proceed up to the kidney. Thus, urinary retention produces increased susceptibility of the urinary tract to infection. Creevy says, "The necrotic tissue furnishes a culture medium the surface of which is isolated from the usual defenses against bacterial invasion; the loss of contractility causes incomplete emptying of the bladder. The resultant stasis favors bacterial growth."

Indeed, this sequence of events was described as early as 1873 by Goodheart.[32] Others (Achard and Regnault,[1] Albarran and Halle,[3] Bazy,[4] Melchior,[48] Rovsing,[64] and Schmidt and Aschoff[65]) have shown that virulent bacteria injected into the intact bladder are harmless until the bladder is traumatized or obstructed, whereupon severe infection of the bladder and upper urinary tract often develops.

When a measurable quantity of urine is present in the bladder, the intravesical tension is 6 to 10 cm. water (Boeminghaus,[7, 8] Mosso and Pellacani,[51] and Rose[61]). When the volume reaches 200 to 400 c.c., the pressure quite abruptly rises to 18 to 30 cm. water, the exact figure being different for different authors (Hirsch,[38] Kreutzmann,[40] Pilcher,[57] Schwarz and Brenner[66]), and a desire to urinate, coinciding with mild rhythmic contractions of the detrusor and relaxation of the internal sphincter, is established.

Received for publication, April 22, 1944.

The human detrusor urinae is probably incapable of exerting a pressure much more than 40 cm. water, the intravesical tension maintaining a fairly constant degree of pressure within wide limits of filling. This ability of the bladder to relax as it fills, maintaining a constant pressure, was designated by Sherrington[68, 69] as "postural tone." However, this pressure is raised remarkably in acute urinary retention, with resulting damage due to the intermittent attempts to void, which may produce considerable rises in intravesical tension (Creevy[22]).

Creevy[24] has pointed out that the inability to void after surgical operations is due to the horizontal position of the patient, the pain of the injured tissues, and drugs, such as the anesthetic or opiate. He has emphasized the importance of early catheterization, if spontaneous voiding six to eight hours after the previous voiding is impossible. He correctly has pointed out the fallacy of relying on cholinergic, vagotropic, or parasympathomimetic drugs or such artifices as audible running water to produce voiding. More often than not, urine so obtained is merely an overflow. A more physiologic emptying may be permitted through a small sterile, well-lubricated catheter, passed gently and frequently enough, or simply left in place for a day.

PURPOSE OF THE STUDY

Although the acute urinary retention secondary to many operations, such as the post-partum state (Bennetts and Judd[6]), and to laparotomies is a familiar picture, no studies have been recorded of the effects of such procedures or the anesthesias per se on the cystometrogram. The measurements to be described were undertaken with the view of determining the relationship between desire to void, intravesical tension at that point, and the bladder volume required in the immediate postanesthetic period.

Varying figures have been published purporting to represent the pressure in the distended bladder. Dubois[28] stated that the pressure was 9 to 10 cm. water; Pilcher[57] gives it as 26 to 30 cm. water; Campbell[15] found the average of eleven cases to be 28 cm. water; Bumpus and Foulds[14] found it to be 50 cm. water. Watkins,[78] using large quantities of filling fluid, found that a progressive rise in bladder pressure took place with filling. From the work of Mellanby and Pratt,[49] and Boyd and Smith,[9] it appears that a progressive rise does not take place under physiologic conditions.

It becomes apparent, then, that one must employ a method of cystometry which would approximate normal conditions. For this purpose ninety-four young men, none of whom had any apparent urologic disease, with ages ranging from 18 to 35 years, were selected. These soldiers were operated on under spinal anesthesia for the conditions listed in Table I, cystometrograms being made as soon as sensation below the level of anesthetic injection returned. Consequently, in

TABLE I

DISTRIBUTION OF OPERATIONS AMONG CASES USED FOR CYSTOMETRIC STUDY

SURGICAL PROCEDURE	NUMBER OF CASES
Spinal Anesthesia	
Hemorrhoidectomy	18
Pilonidal cystectomy	42
Appendectomy	8
Rectopexy	2
Inguinal herniorrhaphy	8
Débridement of foot	2
Hydrocelectomy	2
Anal fistulatomy	4
Curettement, actinomyosis of inguinal region	1
Meniscectomy (knee)	2
Colectomy	1
Preparation of abdominal tubed pedicle graft	1
Pinch grafts from abdomen	3
Total	94
Intravenous Pentothal Sodium Anesthesia	
Incision and drainage of abdominal wall abscess	1
Curettement, actinomycosis of neck	1
Divulsion of anorectum for stricture	1
Manipulation of knee	1
Reduction of dislocated ankle	1
Total	5

nearly every case, the determination was made within two hours after the patient's return from the operating room.

The principles of cystometry and the interpretation of cystometrograms have been adequately discussed elsewhere. (McCrea,[47] Lewis and Langworthy,[43] O'Heeron,[55] Simons,[72] Cheetham,[17] Boyd and Smith,[10] Weyrauch and Peterfy,[79] and Wood.[80]) In addition many types of cystometers have been described (Cone and Bridgers,[19] Valk,[75] Davidson,[26] Simons,[71] Lewis,[42] Povlsen,[58] Brodie, Helfert, and Phifer,[11] Carleton and Nagamatsu,[16] Lich and Ortner,[44] Greenberger and Helfert,[33] Muschat,[53] and Landes and Voris.[41])

The procedure followed in this investigation was similar to that suggested by Rose.[60, 62, 63] A small whistle-tip catheter, No. 12 or 14F, was passed into the bladder and anchored to the penis with a single strip of adhesive tape, the bladder being allowed to empty. The catheter was then attached to the inlet tube (*C*) of the cystometer (Fig. 1) which is a three-outlet Carrel-Dakin tube of the tidal irrigator described previously (Bellis[5]). The Murphy drip (*D*) permits a continuous flow of measurable quantities of saturated boric acid solution from the reservoir (*R*) at the rate of about four drops per second, which is roughly equivalent to 15 c.c. per minute. Fluctuations of intravesical pressure, indicative of bladder contractions, are clearly visible in the upright glass manometer tube (*M*). In each case the pressure developed with each 20 c.c. of added fluid was recorded. The intravesical pressure and bladder volume were noted when the patient

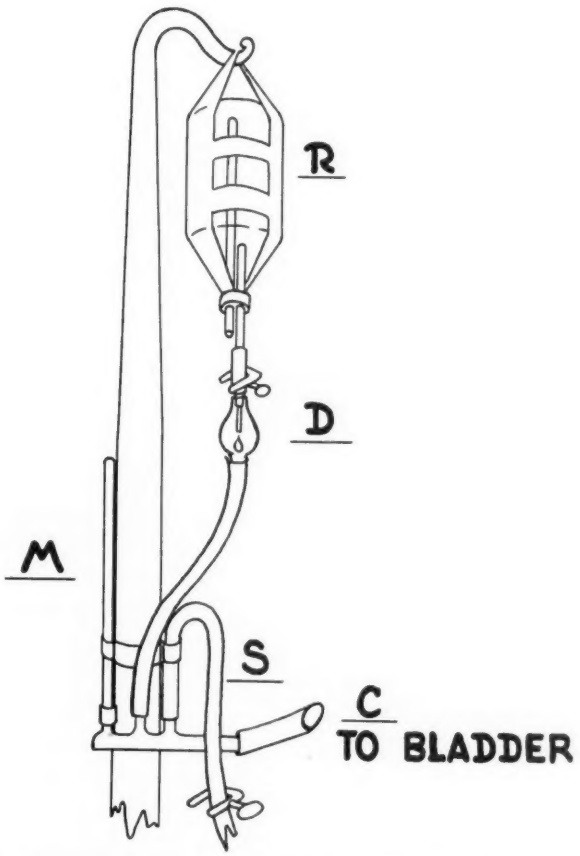


Fig. 1.—Tidal irrigator converted to cystometer. *R*, reservoir; *D*, Murphy drip; *M*, manometer; *S*, siphon; and *C*, catheter tubing.

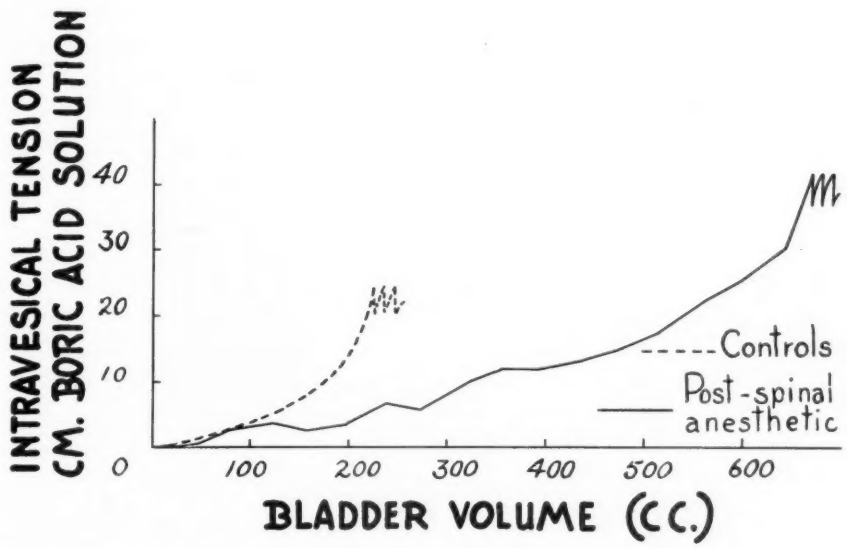


Fig. 2.—Effect of spinal anesthesia on mean intravesical tension developed with increasing bladder volume.

indicated a desire to void, attended by the development of pain and such marked bladder contractions that fluid was expelled around the catheter. The cystometry was then discontinued, the bladder fluid siphoned off (*S*), and the catheter removed. Many of the patients were given injections of morphine during the cystometry because of postoperative pain. Although the cystometrograms in such cases may have been slightly altered by the narcotic, the modification of the readings obtained are probably not important.

Control determinations were made on five patients who had been given intravenous pentothal sodium as anesthesia for very short operations. In these cases, it was necessary that the cystometry be performed in two to three hours postoperatively in order to allow for recovery from the anesthetic.

RESULTS

The study showed a surprising uniformity of measurements. Generally, in the spinal anesthetic group, the intravesical tension increased slowly as the bladder was distended with fluid, the strong rhythmic contractions, indicated by fluctuations in the manometer column, coincident with desire to void, occurring at greater volumes and at higher pressures than in the controls. The mean volume of solution required to produce a desire to void in the spinal series was 671 c.c. the mean intravesical tension at that point being 42 cm. water (Fig. 2). The small rhythmic vesical contractions during filling described by Goltz[31]

TABLE II

MEAN INTRAVESICAL TENSIONS CORRESPONDING TO BLADDER VOLUMES

BLADDER VOLUME (C.C.)	INTRAVESICAL TENSION (CM. BORIC ACID SOLUTION)
Spinal Anesthetic Group	
40	1
80	3
120	4
160	3
200	4
240	7
280	6
320	10
360	12
400	12
440	13
480	14
520	16
560	22
600	25
640	31
671	42
Control Group	
40	2
80	3
120	6
160	9
200	12
224	24

in the dog were also observed in these patients. The greatest volume of solution required to produce strong bladder contractions and a desire to void was 1,340 c.c., the pressure developed being 41 cm. water. The least volume of solution required was 480 c.c., the intravesical tension at that distention being 21 cm. water.

In the control group, the mean bladder volume at which desire to void was experienced was 224 c.c., the mean intravesical tension at that volume being 24 cm. water (Fig. 2). The greatest bladder volume necessary to produce a desire to void was 260 c.c., the tension at that volume being 28 c.c.

In both groups the intravesical tension rose slowly as fluid was added to the bladder. However, as the point where desire to void was approached, the intravesical tension rose rapidly, giving a parabolic, rather than a logarithmic type of curve (Table II).

DISCUSSION

It is well known that lesions of the central nervous system which disturb sensation of the bladder disturb its voluntary control (Curling[25]). Consequently, the use of the cystometrogram in the study of neurogenic vesical dysfunction has received wide recognition (Smith and Engel,[73] Magid,[45] Adams,[2] Voris and Landes,[77] Muschat,[54] and Munro and Hahn[52]). Not one investigator in this field has failed to emphasize that when sensation from the bladder is lost, its postural tonus arcs are interrupted, leading to overdistention with absence of desire to urinate, even at abnormally high intravesical tensions. If this state is allowed to persist even for a few hours, bladder sensation is further obtunded, aggravating the cycle. Shatlock[67] demonstrated a temporary retention and overflow incontinence in the cat after cocainization of the bladder mucosa. More recently, Kirwin and Hawes[39] showed that in six young men who had voided after retaining their urine as long as possible and who were catheterized after finally urinating, residuals of 70 to 365 c.c. were present. Thus, even the vesical distention produced by voluntary retention may produce pressure anesthesia of the bladder wall.

Since the stretch reflex for the bladder is in the sacral cord (Budge,[12, 13] Giannuzzi,[30] and McClintic[46]), it is not surprising that residual vesical effects are found after the use of spinal anesthesia. Rehfisch[59] showed that urinary continence is a matter of mural tonus rather than sphincter action, and although this concept is somewhat modified today from our knowledge of the anatomic disposition of the internal sphincter, it still remains that sphincter action is not the most important mechanism in continence.

Creevy,[23] Gruber,[35] and Hibbs[37] have fully described the innervation of the bladder in relation to micturition. The internal sphincter itself is probably a specialization of the detrusor urinae, while the external

sphincter, lying between the layers of the urogenital diaphragm, consists of the sphincter urogenitalis urethrae and the transversus perinei profundus, contracting as a unit.

The pudic (pudendal) nerves arising from the first three or four sacral segments are sensory for the urethra and motor to the external sphincter. The pelvic nerves (nervus erigens), also arising from the first three or four sacral segments, are parasympathetic and sensory, carrying sensory impulses from the bladder wall and motor impulses to it through the terminal ganglia of the vesical plexus. Being motor to the detrusor, they also cause the internal sphincter to open.

The hypogastric nerves (presacral) are physiologically sympathetic, arising from the second to fifth lumbar segments, proceeding by way of synapses in the inferior mesenteric ganglia and the postganglionic fibers to form the lower ganglia of the abdominal sympathetic trunk. According to Creevy, a few preganglionic fibers from the aortic plexus have synapses in the ganglia of the vesical wall. Although about 25 per cent of the fibers of the hypogastric plexus are sensory, the primary function of the hypogastric nerves is to inhibit the detrusor, and, hence, they have been called the "nerves of bladder filling." Although there may be a myogenic contraction of the detrusor, as seen occasionally in neglected cases of neurogenic vesical dysfunction with overflow incontinence, there are two principal centers for micturition: (1) bilaterally symmetrical in the brain, and (2) in the spinal cord and vesical plexus.

Therefore, urinary retention may be caused by an irritative motor lesion producing sphincter spasm, or it may result from detrusor paralysis, usually from loss of sensation rather than from motor paralysis per se. The result of distention, as seen in overflow incontinence, is a rise of intravesical tension to a destructive level, with dilation of the ureters and kidney pelves, hydronephrotic atrophy, and uremia.

Spinal anesthesia temporarily establishes a type of neurogenic vesical dysfunction, probably due to the anesthetic agent. The bladder wall remains somewhat insensitive to its distending contents, and although the expulsive force of the detrusor may actually not be diminished, the normal strong reflex vesical contractions, which coincide with desire to void, do not appear until the volume of the bladder and the intravesical tension are so great as to invite further pressure anesthesia of the wall, and a continued sensory type of retention which initiates urinary infection.

To wait until the bladder is distended to these levels is to court infection. If malaise, chills, fever, and leucocytosis follow catheterization after the bladder has been so distended, the blame need not be placed on the catheter. The surgeon must call himself to task for allowing the seeds of infection to become implanted in the bladder wall by permitting distention, pressure necrosis, retention, and reduced sensitivity to pursue their vicious cycle. Early catheterization

of patients after administration of spinal anesthesia, and, perhaps, after inhalation anesthesia, is a necessary therapeutic adjunct.

The surgeon must be mindful of the hour at which the bladder was emptied preoperatively, the diuretic effect of the sympathetic-paralyzing anesthetics, and the fluids administered postoperatively. Often, a patient will require catheterization four or five hours after returning from the operating room, where operation, perhaps of one hour, has been performed, and following which intravenous solutions have been administered. Merely to direct a subordinate to "catheterize in twelve hours if patient has not voided," is a fateful and foreboding procrastination. Early catheterization, by preventing pressure anesthesia of the bladder wall, will facilitate early subsequent spontaneous voiding, while delayed or widely-spaced catheterizations serve to aggravate the neurogenic dysfunction and precipitate infection.

SUMMARY

Cystometrograms were made in ninety-four surgical patients immediately after cessation of spinal anesthesia. It was found that the mean volume of solution and the corresponding mean intravesical pressure required to produce desire to void were extremely high (671 c.c. at 42 cm. water) compared with controls having received intravenous anesthesia. In no case were the intravesical volume and tension within normal limits. This is interpreted to mean that following the use of spinal anesthesia there remains a residual mural insensitivity, coexistant with a decrease in vesical tone.

These observations are discussed in the light of the neurophysiology of micturition and the dangers attending delay in catheterization of the postspinal anesthetic patient.

REFERENCES

1. Achard, C., and Regnault, J.: Sur les rapports du Bacterium coli commune avec le Bacterium pyogenes des infections urinaires, Compt. rend. Soc. de biol., Paris **43**: 830, 1891.
2. Adams, P. S.: Use of Cystometer in Diagnosis of Neurogenic Bladders (With Comments on Treatment and Case Reports), Nebraska M. J. **23**: 63, 1938.
3. Albarran, J., and Halle, N.: Note sur une bactérie pyogène et sur son rôle dans l'infection, Bull. Acad. de méd., Paris **20**: 310, 1888.
4. Bazy: Note sur le pathogénie, le diagnostic, et le traitement des pyelonéphrites suppurrées., Bull. et mém. Soc. nat. de chir. **22**: 263, 1896.
5. Bellis, C. J.: An Improved Apparatus for Tidal Drainage of the Urinary Bladder and Empyema Cavities, SURGERY **8**: 791, 1940.
6. Bennetts, F. A., and Judd, G. E.: The Post-Partum Bladder, Am. J. Obst. & Gynec. **42**: 419, 1941.
7. Boeminghaus, H.: Zur Feststellung des Einflusses der Blasenfüllung auf die Funktion der Nieren, Deutsche. med. Wchnschr. **51**: 138, 1925.
8. Boeminghaus, H.: Ueber funktionelle Zusammenhänge zwischen Harnblase und Niere (vesico-renaler Reflex), Arch. f. klin. Chir. **154**: 114, 1929.
9. Boyd, M. L., and Smith, W. A.: Why Are Abnormal Cystometrograms Obtained in Normal Patients? J. Urol. **40**: 513, 1938.
10. Boyd, M. L., and Smith, W. A.: Are Cystometrograms Indispensible for Explanation of Function Disturbances? J. Urol. **42**: 410, 1939.
11. Brodie, E. L., Helfert, I., and Phifer, I. A.: Cystometric Observations in Neurosyphilis, Urol. & Cutan. Rev. **43**: 51, 1939.

12. Budge, J.: Ueber das Centrum genitospinale des Nervus sympathicus, Virchows Arch. f. path. Anat. **15**: 115, 1858.
13. Budge, J.: Zur Physiologie des Blasenschliessmuskels, Arch. f. d. ges. Physiol. **6**: 306, 1872.
14. Bumpus, H. C., Jr., and Foulds, G. S.: Gradual Emptying of the Overdistended Bladder, J. A. M. A. **81**: 821, 1923.
15. Campbell, M. F.: Studies in Bladder Decompression, J. Urol. **17**: 371, 1927.
16. Carleton, S., and Nagamatsu, G. R.: A New Cystometer, J. Urol. **41**: 941, 1939.
17. Cheetham, J. G.: Clinical Evaluation of Cystometer, J. Urol. **39**: 569, 1938.
18. Chute, A. L.: Observations on Cases of Prostatic Obstruction Presenting Overdistended Bladders, Boston M. & S. J. **167**: 607, 1912.
19. Cone, W. V., and Bridgers, W. H.: Combined Tidal Irrigator and Cystometer for Management of the Paralyzed Bladder, Surg., Gynec. & Obst. **75**: 61, 1942.
20. Creevy, C. D.: Sudden Decompression of the Chronically Distended Urinary Bladder, Arch. Surg. **25**: 356, 1932.
21. Creevy, C. D.: Distention of the Urinary Bladder. I. Hematuria and Sudden Emptying; an Experimental and Clinical Study, Arch. Surg. **28**: 948, 1934.
22. Creevy, C. D.: Vesical Distention. Effects on the Motor Mechanism of the Upper Urinary Tract; An Experimental Study, Arch. Surg. **29**: 723, 1934.
23. Creevy, C. D.: Neurogenic Vesical Dysfunction. Alterations in the Physiology of Micturition Due to Lesions of the Nervous System, Arch. Neurol. & Psychiat. **34**: 777, 1935.
24. Creevy, C. D.: The Care of the Urinary Bladder After Operation, SURGERY **7**: 423, 1940.
25. Curling, H. B.: Affections of the Urinary Bladder in Paraplegia, London Med. Gaz. **13**: 353, 1833.
26. Davidson, O. W.: A Practical Cystometer, J. Urol. **40**: 452, 1938.
27. Delbet, P.: Rétention et incontinence d'urine; in Pousson, A., and Desnos, E.: Encyclopédie française d'urologie, vol. 6, Paris, 1914, Gaston Doin & Cie, p. 492.
28. Dubois, P.: Ueber den Druck in der Harnblase, Deut. Arch. f. klin. Med. **17**: 148, 1876.
29. Genouville, M., and Boeckel, A.: Physiologie pathologique du cathétérisme: in Pousson, A., and Desnos, E.: Encyclopédie française d'urologie, vol. 4, Paris, 1914, Gaston Doin & Cie, p. 944.
30. Giannuzzi: Recherches physiologiques sur les nerfs moteurs de la vessie, J. physiol. de l'homme. **6**: 22, 1863.
31. Goltz, F.: Ueber die Funktionen des Lendenmarks des Hundes, Arch. f. d. ges. Physiol. **8**: 460, 1874.
32. Goodheart, J. F.: On Erysipelas of the Kidney and Urinary Tract, Guy's Hosp. Rep. **19**: 357, 1873.
33. Greenberger, M. E., and Helfert, I.: Cystometric Observations in Tuberculous Bladders, Quart. Bull., Sea View Hosp. **5**: 415, 1940.
34. Grellety, M.: Mécanisme des accidents mortels qui dans certains cas accompagnent l'évacuation trop prompte de la vessie, France méd. **25**: 146, 1879.
35. Gruber, C. M.: The Autonomic Innervation of the Genito-Urinary System, Physiol. Rev. **13**: 497, 1933.
36. Guyon, J. F., and Albarran, J.: Anatomie et physiologie de la rétention d'urine, Arch. de méd. expér. et d'anat. **2**: 181, 1890.
37. Hibbs, D. K.: Physiology of Micturition, Urol. & Cutan. Rev. **43**: 257, 1939.
38. Hirsch, E. W.: Relation of Bladder Pressure to Bladder Function, J. A. M. A. **91**: 772, 1928.
39. Kirwin, T. J., and Hawes, G. A.: The Diagnostic Value of Residual Urine Examinations, J. Urol. **41**: 413, 1939.
40. Kreutzmann, H. A. R.: Studies in Normal Ureteral and Vesical Pressure, J. Urol. **19**: 517, 1928.
41. Landes, H. E., and Voris, H. C.: A New Cystometer, Incorporating Advantage of Water Manometer and Continuous Tracing, J. Urol. **39**: 813, 1938.
42. Lewis, L. G.: A New Clinical Recording Cystometer, J. Urol. **41**: 638, 1939.
43. Lewis, L. G., and Langworthy, O. R.: Cystometry, J. Urol. **40**: 677, 1938.
44. Lich, R., Jr., and Ortner, A. B.: Economical Two-Way Catheter for Cystometry, Urol. & Cutan. Rev. **44**: 616, 1940.
45. Magid, M. A.: Value of Cystometric Studies in Atonic Bladder, Rocky Mountain M. J. **35**: 299, 1938.
46. McClintic, C. F.: The Clinical Neurophysiology of the Autonomic Urinary Bladder and Enureses, J. Urol. **20**: 267, 1928.
47. McCrea, L. E.: Cystometry and Its Interpretation, Urol. & Cutan. Rev. **44**: 362, 1940.

48. Melchior, M.: Berichte über 52 bakteriologische untersuchte Fälle von infectiöse Erkrankungen der Harntracte, Monatsb. d. Krankh. d. Harn. u. Sex.-Appar. **3**: 584, 1898.
49. Mellanby, J., and Pratt, C. L. G.: Reactions of Bladder of Cat Under Conditions of Constant Pressure, Proc. Roy. Soc., London, s. B. **127**: 307, 1939.
50. Mercier, A.: Note sur l'hématurie qui suit le cathétérisme dans quelques cas de rétention d'urine, Union. med. de Paris **9**: 41, 1861.
51. Mosso, A., and Pellacani, P.: Sur les fonctions de la vessie, Arch. ital. de biol. **1**: 97, 291, 1882.
52. Munro, D., and Hahn, J.: Tidal Drainage of the Urinary Bladder, New England J. Med. **212**: 229, 1935.
53. Muschat, M.: Simplified Determination and Practical Interpretation in Cystometry; Critique of Attempts Made to Complicate This Procedure, J. Urol. **43**: 582, 1940.
54. Muschat, M.: Cystometric Timing of Catheter Removal From a Neurogenic Bladder, SURGERY **7**: 710, 1940.
55. O'Heeron, M. K.: Cystometry; Value and Limitations, J. Urol. **47**: 824, 1942.
56. Picard, M.: Les dangers du cathétérisme chez les viellards, France méd. **26**: 106, 1879.
57. Pilcher, P. M.: Prostatectomy in Two Stages, Ann. Surg. **59**: 500, 1914.
58. Povlsen, O.: Cystometric Technik, Ztschr. f. urol. Chir. u. Gynäk. **45**: 72, 1939.
59. Rehfisch, E.: Ueber den Mechanismus des Harnblasenverschlusses und der Harnentleerung, Virchows Arch. f. path. Anat. **150**: 111, 1897.
60. Rose, D. K.: Cystometric Bladder Pressure Determinations, J. Urol. **17**: 487, 1927.
61. Rose, D. K.: Clinical Application of Bladder Physiology, J. Urol. **26**: 91, 1931.
62. Rose, D. K.: Various Cystometrograms and Their Interpretation, J. Urol. **27**: 207, 1932.
63. Rose, D. K.: An Improved Continuous Flow Recording Cystometer, J. Urol. **43**: 718, 1940.
64. Rovsing, T.: Aetiologie, Pathogenese, und Behandlung der septic Infektion der Harnwege, Monatsb. d. Krankh. d. Harn. u. Sex.-Appar. **3**: 506, 1898.
65. Schmidt, M. B., and Aschoff, L.: Die Pyelonephritis in anatomscher und bakteriologischer Beziehung und die ursächliche Bedeutung der Bakterium coli commune für die Erkrankung der Harnwege, Jena, 1893, Gustav Fischer.
66. Schwarz, O., and Brenner, A.: Untersuchungen ueber die Physiologie und Pathologie der Blasenfunktion, Ztschr. f. urol. Chir. **8**: 32, 1921.
67. Shatlock, S. G.: Is There an Idiopathic Dilatation of the Urinary Bladder? Proc. Roy. Soc. Med. (Sect. Path.) **2**: 88, 1908.
68. Sherrington, C. S.: The Lumbo-Sacral Plexus, J. Physiol. **13**: 678, 1892.
69. Sherrington, C. S.: Postural Activity of Muscle and Nerve: ii Visceral Muscle, Brain **38**: 213, 1915.
70. Shigematsu, H.: Etude expérimentelle de la retention d'urine, J. d'urol. **25**: 16, 1922.
71. Simons, J.: Neurologic Studies by Means of Microcystometer and Sphincterometer; Studies in Bladder Function (preliminary report), J. Urol. **39**: 791, 1938.
72. Simons, J.: Cystometry; Status and Outlook, With Special Reference to Microcystometry and Sphincterometry, Urol. & Cutan. Rev. **42**: 316, 1938.
73. Smith, C. K., and Engel, L. P.: Neurogenic Vesical Dysfunction in Children, J. Urol. **28**: 675, 1932.
74. Tuffier, T.: Rôle de la congestion dans les maladies des voies urinaires, Thèse de Paris, 1885, p. 149.
75. Valk, W. L.: A Simple and Inexpensive Cystometer, J. Urol. **47**: 838, 1942.
76. Vintici, V., and Laroche, A.: Hemorrhagies de la prostate, J. d'urol. **28**: 140, 1929.
77. Voris, H. C., and Landes, H. E.: Cystometric Studies in Cases of Neurologic Disease, Arch. Neurol. & Psychiat. **44**: 118, 1940.
78. Watkins, K. H.: The Clinical Value of Bladder Pressure Estimations, Brit. J. Urol. **6**: 104, 1934.
79. Weyrauch, H. M., Jr., and Peterfy, R. A.: Tests for Leakage in Early Diagnosis of Ruptured Bladder; Use of Cystometrogram, J. Urol. **44**: 264, 1940.
80. Wood, L. G.: Cystometry, Bull. Vancouver M. A. **17**: 299, 1941.

A DEMONSTRATION OF TWO TYPES OF BURN SHOCK

MYRON PRINZMETAL, M.D., H. C. BERGMAN, PH.D., AND
OSCAR HECHTER, PH.D., LOS ANGELES, CALIF.

(From the Straus Research Laboratory, Cedars of Lebanon Hospital, and the University of Southern California Medical School)

IT HAS been recently shown that shock due to muscle injury can be produced through at least two different mechanisms: (1) local fluid loss, as demonstrated by Blalock,[1] and (2) a toxic factor, bacterial in origin.[2] It seemed important to determine whether shock due to varying types of burns might not similarly result from more than one mechanism, depending upon the characteristics of the burn.

The principal evidence for the view that burn shock may result from local fluid loss is based upon the work of Blalock[1] and Harkins[3] who found by actual measurement that considerable local fluid loss occurs in and near the burned areas. The degree of local fluid loss which they found was considered sufficient to account for some or all of the deleterious effects in early burn shock. The significance of their results will be discussed later.

In the course of extensive investigation on burn shock, we, as well as Elman and Lischer[4] have observed that following a slight burn marked edema occurs, whereas with more severe burns the amount of visible edema appears to be considerably less. As a result of this observation, we decided to investigate the degree of local fluid loss in various types of burns and to determine whether or not there was a correlation between the occurrence of shock and the degree of local fluid loss.

METHODS

Two types of burns were produced in the following ways: (1) A mild burn involving a small part of the body surface was produced in sixty rats by immersing a single hind limb of the etherized animal up to the hip in water at 75° C. for ten seconds. The area burned was approximately 7 per cent of the body surface as determined by postmortem dissection. (2) A severe burn involving the same small area was produced by immersing the hind limb of twenty-seven chloroformed rats into boiling water for from two to three minutes.

The animals were not given food or water after the burning procedure.

The fluid shifts in burned animals were evaluated on the basis of bisection studies, using a method previously described by Hechter and co-workers.[5] After determining the body weight, midline skin incisions extending from the head to the tail were made upon the

Aided by grants from the Blanche May Selden Fund, the Martha Kirschner Haft Memorial Fund, F. Brice, and Morton May.

Received for publication, May 4, 1944.

ventral and dorsal surfaces of the animal. The thoracic and abdominal contents were then removed and the carcass weight determined. The lower portion of the body was divided from the upper half by cutting through all of the tissue layers and the spinal column on a line parallel to, and just below, the lowest ribs of the thoracic cage. The vertebral column and the tail were then removed by careful

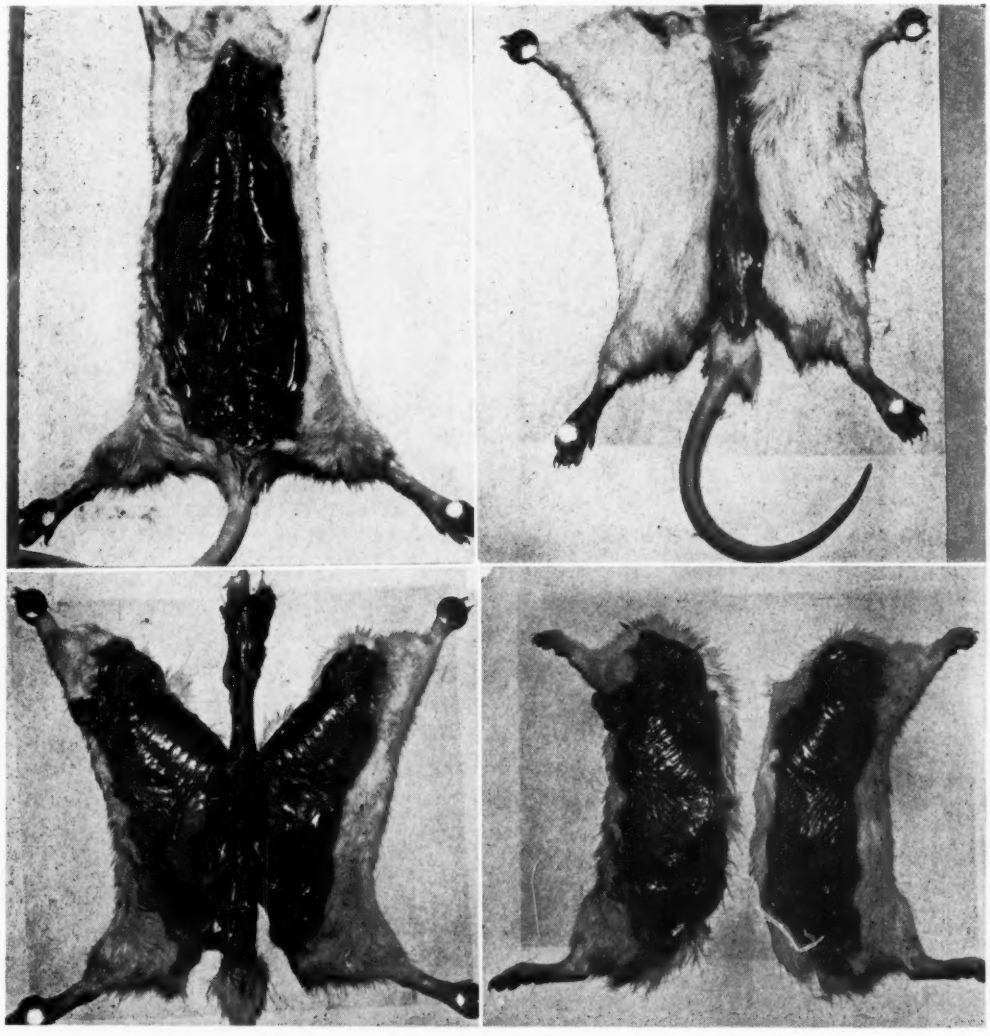


Fig. 1.—Method of bisection. The last step is not shown, which involves separation of the lower quadrants by an incision paralleling the lowest rib.

dissection, thus separating the two lower extremities. By comparing the weight of the burned side with that of the nonburned side of the animal, the degree of fluid shift evaluated as per cent of the body weight was measured (Fig. 1).

The accuracy obtainable with this method of bisection is illustrated in Table I where the results obtained on twelve consecutive measure-

TABLE I

THE VARIATION BETWEEN THE TWO LOWER QUADRANTS OF NONBURNED RATS, USING THE BISECTION METHOD

EXP. NO.	RAT BODY WEIGHT (GM.)	RIGHT LEG	LEFT LEG	DIFFERENCE (GM.)	DIFFERENCE AS PER CENT OF BODY WEIGHT
1	240	33.1	32.0	1.1	0.5
2	207	25.0	23.5	1.5	0.7
3	250	53.3	53.7	0.4	0.2
4	240	34.9	33.7	1.2	0.5
5	180	24.4	25.6	1.2	0.8
6	170	24.6	24.8	0.2	0.1
7	164	23.3	23.7	0.4	0.2
8	156	22.0	23.7	1.7	1.1
9	177	26.2	24.8	1.4	0.8
10	138	19.5	20.0	0.5	0.4
11	197	28.2	29.0	0.8	0.4
12	151	22.1	22.3	0.2	0.1

ments on nonburned animals are shown. It will be seen that the difference between the two lower quadrants varied from 0.1 to 1.1 per cent of the body weight (0.2 to 1.7 Gm.), the average being 0.5 per cent. These variations of the method of bisection for rats are in the same range as those reported by Blalock[1] in dogs.

RESULTS

Slight Burn Involving Small Surface of the Body.—Animals receiving a 75° C. burn for ten seconds involving one limb remained in excellent condition and never went into shock. The limb, and especially the paw, became markedly edematous and on incision exuded fibrinous fluid (Fig. 2). In order to determine how rapid the fluid accumulated, animals were sacrificed one, five, twenty-four and forty hours after this burn. The degree of local fluid loss is shown graphically in Fig. 3. It will be seen that animals lose, on the average, 2 per cent of their body weight into the burned quarter at one hour; 3.3 per cent at five hours; 3.9 per cent at twenty-four hours; and 3.8 per cent at forty hours after thermal injury. It is of importance to observe that seven animals lost 5 per cent or more of their body weight in fluid and yet remained in excellent condition, not developing shock. The results demonstrate three things: First, a slight burn involving a small area of the body surface produces considerable local fluid loss but does not lead to the development of shock; second, most of the local fluid loss with this burn occurs very rapidly, as Harkins[3] has also demonstrated; third, animals can lose over 5 per cent of their body weight locally and do not develop shock if the loss takes place slowly.

Severe Burn Involving Small Surface.—The findings with the slight burn are in striking contrast to the results obtained in animals in which a severe burn was produced over the same area of the body surface involving one extremity. It was observed with the 100° C. burn that the burned limb became hard and pale. Visible local edema in the

Fig. 2.—Right hind limb of rat burned at 75° C. for ten seconds showing marked edema of the right limb. Animals with this mild degree of burn do not go into shock.

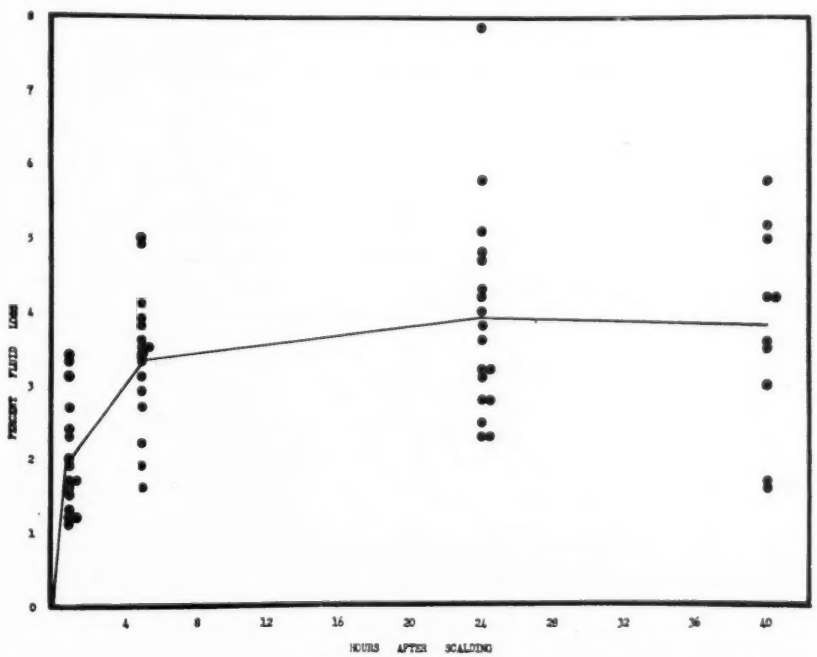


Fig. 3.—Local fluid loss obtained in sixty rats burned at 75° C. for ten seconds on one hind limb. These animals did not go into shock.

Fig. 4.—Right hind limb of rat burned at 100° C. for two minutes. The limb is shrunken and does not appear edematous. Animals burned in this manner with little local fluid loss exhibited shock (thirteen of twenty-seven died).

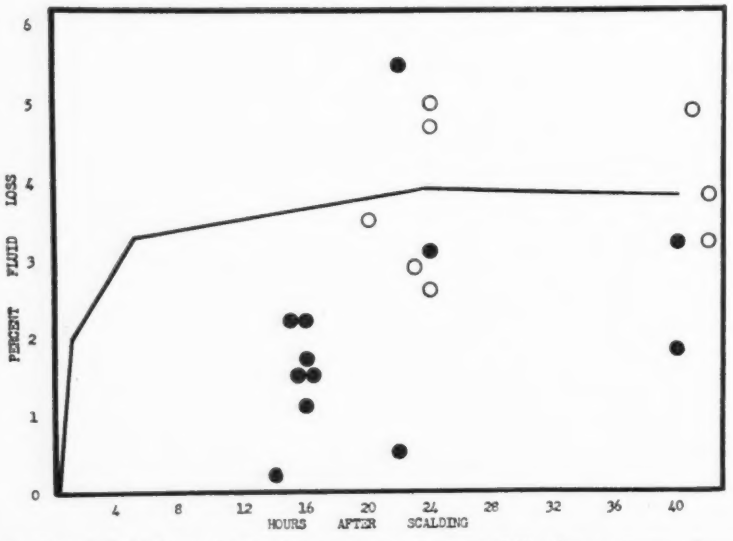


Fig. 5.—Local fluid loss obtained in twenty-six rats following a burn of one hind limb at 100° C. for from two to three minutes. The dots represent animals that died in shock. The circles represent animals that were killed at the times shown. The curve is the average fluid loss represented in Fig. 3, demonstrating the degree of fluid loss of animals not going into shock. Eleven of the twelve animals that died had less fluid loss than was found in mildly burned animals not going into shock.

TABLE II

THE FLUID SHIFT INTO A HIND LIMB BURNED AT 100° C. FOR FROM TWO TO THREE MINUTES

TIME OF DEATH OR KILLING AFTER BURN (HR.)	DIED OR KILLED	RAT BODY WEIGHT	NORMAL LEG WEIGHT	BURNED LEG WEIGHT	DIFFERENCE IN WEIGHT (GM.)	DIFFERENCE AS PER CENT OF BODY WEIGHT
14	Died	193	34.7	35.2	0.5	0.2
16	Died	326	53.1	60.4	7.3	2.2
16	Died	176	37.6	40.5	2.9	1.7
16	Died	207	39.7	42.9	3.2	1.5
16	Died	162	25.0	27.4	2.4	1.5
16	Died	200	35.7	37.9	2.2	1.1
16	Died	175	30.5	34.3	3.8	2.2
22	Died	166	29.8	30.6	0.8	0.5
22	Died	236	41.0	55.0	14.0	5.5
24	Died	170	27.3	32.6	5.3	3.1
40	Died	185	32.6	38.6	6.0	3.2
40	Died	183	31.1	34.4	3.3	1.8
20	Killed	163	27.5	33.2	5.7	3.5
23	Killed	166	28.1	33.0	4.9	2.9
24	Killed	149	23.0	30.0	7.0	4.7
24	Killed	368	54.2	72.7	18.5	5.0
24	Killed	195	35.8	40.8	5.0	2.6
47	Killed	180	28.8	34.5	5.7	3.2
48	Killed	171	30.0	36.5	6.5	3.8
43	Killed	199	31.0	40.9	9.9	4.9

burned extremity was not evident (Fig. 4). These animals appeared to be in shock and 13 of 27 died within forty hours. The average local fluid loss of 12 of these animals (excluding one because the burned limb was chewed off) was 2.05 per cent of the body weight. The degree of local fluid loss was greater in the 14 animals that did not die but were sacrificed after forty hours than in those that died in shock, the average being 3.7 per cent (Fig. 5 and Table II).

These results demonstrate that severely burned animals die in shock with less local fluid loss than that observed in slightly burned animals not going into shock. Similarly, in the second experiment, the animals that died following a severe burn exhibited less local fluid loss than those surviving the same burn.

DISCUSSION

Blalock[1] and Harkins[3] have shown that fluid loss in and near the burned area is an important factor in the development of burn shock. In this report, it has been clearly demonstrated that animals may die in shock with insignificant local fluid loss following a severe burn. It has been shown that animals mildly burned, not developing shock, exhibit greater local fluid loss than the animals dying from severe burns. Similarly it has been shown that the animals which survived the severe burn exhibited considerably greater local fluid loss than those rats which succumbed. It is therefore apparent that following certain types of burns, animals may die in shock not due to local fluid loss. We have also found in studying 64 animals that were burned

(over 30 to 39 per cent of their body surfaces for ten seconds at 100° C.) that death may occur with insufficient local fluid loss.

The mechanism of death of those animals dying without significant local fluid loss is unknown. It would be useless to speculate on the importance of neurogenic or toxic factors without further evidence. The finding of little local fluid loss does not indicate that the effective circulating blood volume in these animals was not reduced. We are now studying this problem.

In view of our results it would appear probable that Blalock[1] and Harkins[3] might have obtained considerably greater fluid loss with less shock by employing a smaller degree of burn, since the burns they employed were more severe than those used in our experiments where little fluid loss was encountered. It is of interest to observe that Harkins, who used a Bunsen burner for ten minutes, observed less fluid loss than did Blalock, who presumably obtained a lesser degree of thermal injury with hot irons.

It is apparent that in view of these results, therapeutic measures successful in the treatment of one type of burn shock are not necessarily effective in other types. For the past three years we have intensively studied the burn shock which results from scalding 80 to 90 per cent of the body surface of rats and mice for ten seconds at 65 or 75° C.[6] It appears likely that the shock produced by this method is due in large part, at least, to local fluid loss, since we have shown in this study the large amount of fluid which can accumulate into a single limb burned in this manner. If shock from burns is ever due to local fluid loss alone, it should occur under these circumstances, which are more favorable for the production of local fluid loss than any others with which we are acquainted. This might be the explanation for the unusual results originally found by Rosenthal[7] and confirmed by us,[8] that the therapeutic effect of plasma could be accounted for entirely by its sodium content. It has been recently shown by Fox[9] that the amount of sodium in a mildly burned area is disproportionately high, and it is thought that the depletion of sodium from the rest of the body may be an important factor in the development of shock. This offers an explanation for the therapeutic effect of sodium salts in the type of shock found in widespread mild burns. It would appear probable that the sodium factor is less important in shock due to severe burns with insignificant local fluid loss, because it seems likely that the characteristics of the burn which reduce fluid loss would be expected to reduce sodium loss as well. Thus, it is possible that plasma may prove to be superior to saline solution in the type of burn shock with insufficient local fluid loss, as it is in the case in other types of traumatic shock. Likewise, agents effective in the shock due to local fluid loss may be ineffective in the other type of burn shock. Thus, liver extract[6] and sodium salts[7] effective in one type may not be effective in the second type.

It is extremely likely that in clinical burns both factors are of importance and may operate simultaneously in varying degrees. In more severe burns the factor of local fluid loss would appear to be less important, whereas with more widespread mild burns, which produce marked edema and weeping of the skin, the local fluid loss factor may play a greater role. It might be pointed out that patients with widespread severe sunburn with a great deal of local swelling do not as a rule go into shock. Considering the results obtained in this study, it appears to us that the role of local fluid loss in clinical shock from burns may have been overemphasized.

We do not mean to imply from this study that there are only two types of burn shock. It is possible and extremely probable that other factors as yet unknown are implicated. In fact, it is possible that the second "type" without local fluid loss is due to more than one mechanism. The pathogenesis of this type of shock is now being investigated.

CONCLUSIONS

1. Rats who were mildly burned at 75° C. for ten seconds on a single hind limb developed marked visible edema with considerable local fluid loss but did not develop shock.

2. Rats whose single hind limbs were severely burned at 100° C. for from two to three minutes died in shock without visible edema and exhibited insufficient local fluid loss to account for death. Similar results have been obtained when larger areas of the body were severely burned for ten seconds.

3. It is therefore apparent that there are at least two mechanisms capable of producing shock: one due to local fluid loss and the other due to some unknown factor(s).

4. This difference in the mechanism of production of burn shock may explain some of the differences of opinion regarding therapeutic agents in burns.

REFERENCES

1. Blalock, A.: Principles of Surgical Care: Shock and Other Problems, St. Louis, 1940, The C. V. Mosby Co.
2. Prinzmetal, M., Freed, S. C., and Kruger, E.: The Pathogenesis and Treatment of Shock Resulting From Crushing of Muscle, War Med. **5**: 74, 1944.
3. Harkins, H. N.: The Treatment of Burns, Springfield, Ill., 1942, Charles C Thomas.
4. Elman, R., and Lischer, C.: Local Skin Lesion in Experimental Burns and Its Relation to Systemic Manifestations, Surg., Gynec. & Obst. **78**: 346, 1944.
5. Hechter, O., Krohn, L., and Harris, J.: Role of Adrenals in Production of Traumatic Shock in Rats, Endocrinology **31**: 439, 1942.
6. Prinzmetal, M., Hechter, O., Margoles, C., and Feigen, G.: A Principle From Liver Effective Against Shock Due to Burns, J. A. M. A. **122**: 720, 1943.
7. Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock. Effects of Systemic Therapy on Early Mortality, Pub. Health Rep. **58**: 513, 1943.
8. Prinzmetal, M., Bergman, H. C., and Hechter, O.: In preparation.
9. Fox, C. L., Jr.: Personal communication.

FURTHER STUDIES ON THE ROLE OF BACTERIA IN SHOCK DUE TO CRUSHED MUSCLE IN DOGS*

S. C. Freed, M.D., H. E. Kruger, and Myron Prinzmetal, M.D.
San Francisco, Calif.
(From the Harold Brunn Institute, Mount Zion Hospital)

In a recent publication from this laboratory,[1] a technique was reported by which shock could be regularly produced in dogs by crushing a known amount of muscle with minimal loss of blood. It was shown that the shock thus produced was a direct result of bacterial action. For it was observed that despite strict, aseptic surgical technique, the crushed muscle was always grossly contaminated. If, however, the bacteria were inhibited by the use of antibacterial agents, shock did not occur and all animals remained in excellent clinical condition. In these experiments sulfamerazine was administered both locally and systemically. In addition, in one group of animals the crushed muscle was soaked in acriflavine solution as was first performed by Abraham and his associates,[2] with intraperitoneal implantation of liver tissue. Untreated animals were obviously in shock at the end of twenty-four hours, there was a decrease in circulating blood volume, the limb operated upon was decidedly swollen, the crushed muscle at autopsy always had a foul odor, gas was often present, and direct smear of the muscle revealed numerous bacteria of many types. This was in striking contrast to the treated animals in which a decrease in blood volume was infrequent, less swelling of the operated quarter was observed, and the crushed muscle at autopsy appeared clean, had no odor, and revealed few or no organisms in direct smear. Despite the considerable swelling of the leg in the untreated animals, it was demonstrated that the local fluid loss was insufficient to account for the shocklike state, and it was concluded that this was an example of toxic shock, as distinguished from extravasative shock induced by other methods such as blows or certain types of burns.

In the first report,[1] it was shown that the systemic administration of sulfamerazine immediately after trauma prevented the occurrence of shock. The following problems seemed of practical importance: How late can the sulfamerazine be administered and still be effeffective? When administered systemically, does the sulfamerazine penetrate into the ischemic, crushed muscle and in what concentration? What is the relative efficiency of local as compared with systemic administration of the drug?

*Aided by a grant from the Columbia Foundation for Medical Research.
Received for publication, June 10, 1944.

Experiment 1. The Local Application of Sulfamerazine.—In eleven dogs the sulfamerazine was administered locally in the following manner. The drug was thoroughly mixed with the crushed muscle before reinsertion. The dosage was 0.5 Gm. of sodium sulfamerazine per 10 Gm. of muscle. No other treatment was given. Nine dogs remained in excellent condition and only two went into shock and died. There was no decrease in blood volume in the animals not going into shock.

It should be emphasized that, in this experiment, the animals received only one administration of the drug and were given no additional therapy. The blood concentration of sulfamerazine was very low (2.5 to 3.5 mg. per cent) and at times only a trace was found.

It appears that the local administration of sodium sulfamerazine was moderately beneficial since shock did not occur in nine out of eleven animals. It is, therefore, apparent that local treatment alone may not be completely effective.

Experiment 2. The Systemic Administration of Sulfamerazine Six Hours After Trauma.—Ten dogs received sodium sulfamerazine (0.2 Gm. per kilogram body weight) intravenously six hours after reinsertion of the crushed muscle. Subsequent daily doses (0.1 Gm. per kilogram body weight) were given orally. The average sulfamerazine blood level of these ten animals was 15.2 mg. per cent, ranging from 9.2 to 20.8 mg. per cent. All ten animals remained in good condition and in seven of the dogs there was no significant change in circulating blood volume (Table I). The wounds of these animals at autopsy appeared clean and had no odor. Cultures of the crushed muscle were sterile in

TABLE I

EFFECT ON BLOOD VOLUME OF CRUSHED MUSCLE OF DOGS RECEIVING SULFAMERAZINE SIX HOURS AFTER TRAUMA

DOG NO.	WEIGHT (KG.)	WT. OF CRUSHED MUSCLE (GM.)	TIME (HR.)	HEMATOCRIT (% R.B.C.)	PLASMA VOLUME (C.C.)	BLOOD VOLUME (C.C.)	OUTCOME
1	6.8	34.6	0	---	463.0	----	No shock
			24	46.0	429.0	794.0	
2	8.2	34.7	0	33.5	424.0	638.0	No shock
			24	34.5	428.0	652.0	
3	5.9	35.7	0	---	397.0	----	No shock
			24	30.5	293.0	422.0	
4	5.4	17.7	0	30.0	477.0	681.0	No shock
			24	31.5	458.0	669.0	
5	12.8	53.4	0	40.0	467.0	778.0	No shock
			24	35.5	514.0	796.0	
6	10.9	51.3	0	36.0	639.0	997.0	No shock
			24	38.0	546.0	880.0	
7	9.5	49.3	0	36.0	477.0	746 0	No shock
			24	37.5	560.0	896.0	
8	6.8	30.0	0	38.0	364.0	587.0	No shock
			24	35.5	377.0	585.0	
9	10.0	40.0	0	32.0	816.0	1200.0	No shock
			24	44.5	440.0	794.0	
10	9.1	37.5	0	35.5	482.0	748.0	No shock
			24	38.0	257.0	415.0	

three, in the remainder the muscle was contaminated but had fewer organisms than the crushed muscles of untreated animals.

It is concluded that the systemic administration of sulfamerazine in adequate doses is completely successful in preventing shock when administered six hours after trauma.

Experiment 3. The Systemic Administration of Sulfamerazine Seventeen Hours After Trauma.—Ten dogs received sodium sulfamerazine (0.2 Gm. per kilogram body weight) intravenously sixteen to eighteen hours after reinsertion of the crushed muscle. Subsequent daily doses (0.1 Gm. per kilogram body weight) were given orally. The average sulfamerazine blood level of these animals was 10.0 mg. per cent, with a range of from 7.4 to 13.2 mg. per cent. Shock developed in five of the dogs, three of which died within seventy-two hours. The reductions in blood volume of these animals are recorded in Table II. The wounds of all of these dogs had an unpleasant odor and culture of the muscle at autopsy revealed contamination.

TABLE II

EFFECT ON BLOOD VOLUME OF CRUSHED MUSCLE OF DOGS RECEIVING SULFAMERAZINE SEVENTEEN HOURS AFTER TRAUMA

DOG NO.	WEIGHT (KG.)	WT. OF CRUSHED MUSCLE (GM.)	TIME (HR.)	HEMATOCRIT (% R.B.C.)	PLASMA VOLUME (C.C.)	BLOOD VOLUME (C.C.)	OUTCOME
1	11.8	60.3	0	39.0	840.0	1377.0	Died 24 hr.
			24	---	----	----	
2	9.5	50.5	0	37.0	570.0	840.0	Shock but
			24	38.0	----	----	recovered
3	8.6	61.1	0	36.0	559.0	872.0	Shock but
			24	32.0	380.0	560.0	recovered
4	7.3	39.0	0	30.0	361.0	515.0	Died 24 hr.
			24	---	----	----	
5	5.5	23.4	0	27.0	387.0	545.0	No shock
			24	27.0	386.0	544.0	
6	9.1	43.2	0	35.0	377.0	580.0	Died 36 hr.
			24	40.0	357.0	595.0	
7	10.5	62.1	0	40.5	573.0	964.0	Shock but
			24	42.0	536.0	924.0	recovered
8	8.6	25.5	0	28.0	840.0	1166.0	No shock
			24	25.0	672.0	866.0	
9	9.1	60.0	0	36.5	622.0	980.0	No shock
			24	32.0	318.0	468.0	
10	9.1	57.0	0	34.0	662.0	1003.0	No shock
			24	35.5	434.0	670.0	

It would seem that sulfamerazine therapy is only of moderate benefit when given as late as seventeen hours after injury.

Experiment 4. The Systemic Administration of Sulfamerazine Twenty-four to Twenty-six Hours After Trauma.—Eleven dogs received sulfamerazine therapy as described, the initial dose being given intravenously twenty-four to twenty-six hours postoperatively. All eleven of these animals went into shock and five died. At autopsy, the wounds of

these animals had a foul odor and cultures revealed heavy bacterial growth.

It should be mentioned that all animals were in shock at the end of twenty-four hours when sulfamerazine therapy was begun. It, therefore, appears clear that sulfamerazine has no therapeutic effect when administered twenty-four hours after trauma.

Experiment 5. Concentration of Sulfamerazine in Blood and Tissues of Dogs Subjected to Muscle Crushing.—Determinations of sulfamerazine were done in the blood, the crushed muscle, and the normal muscle of animals in the preceding experiments.

In Experiment 1, when the drug was administered locally only, the blood concentration twenty-four hours later was between 2.5 and 3.5 mg. per cent; four days later at autopsy only a trace was found in the blood and the normal muscle, while the crushed muscle contained between 1,000 and 2,000 mg. per 100 Gm. of dry tissue.

In animals treated by the systemic administration of sulfamerazine in this and the previous report, it was found that the average blood level of twenty-two dogs was 11.6 mg. per cent with a range of from 6.3 to 20.8 mg. per cent. In twenty-two out of twenty-four instances the concentration of the sulfamerazine in the crushed muscle was higher than that in the normal muscle of the same animal. The average concentration in crushed muscle of twenty-four animals was 62.1 mg. per cent with a range of from 14.3 to 161.5 mg. per cent. The average concenteration in the normal muscle of twenty-two dogs was 23.5 mg. per cent with a range of from 5.5 to 38.5 mg. per cent (Table III).

It is of interest that following systemic administration of sulfamerazine, the ischemic, traumatized tissue contains considerably higher concentration in the normal muscle of twenty-two dogs was 23.5 mg. This fact, the explanation of which is not entirely understood, would appear to be significant because the drug accumulates in high concentration in areas where it is most needed in spite of such areas being unconnected with the systemic circulation.

DISCUSSION

An attempt was made to determine: (1) How long after trauma the administration of sulfamerazine is effective in the prevention or treatment of toxic shock in dogs, and (2) the most appropriate method of administration.

It was found that the local application of this drug without subsequent systemic administration might be effective but is not completely so because an adequate blood concentration is not maintained. The systemic administration of sulfamerazine was found to be the most effective. In the previous study it was shown that this drug completely prevents shock when administered immediately after trauma. In the

present study, it was demonstrated that therapy may be begun six hours after trauma and, with the establishment and maintenance of a high blood level of the drug, shock is completely prevented. If a delay of seventeen hours takes place before sulfamerazine is given, the onset of shock is not prevented but its further development may be arrested, and it would seem that the drug may be of some benefit when administration is begun after seventeen hours. Sulfamerazine therapy, if begun later than twenty-four hours after trauma, seems to be ineffective even though a high blood level is established. It is interesting to note that this time relationship holds true for the débridement experiments reported in our previous study.[1] In the animals treated with sulfamerazine twenty-four hours after trauma, shock was well advanced and the dogs died shortly thereafter. It is possible that if these animals could be brought out of shock by the use of plasma, allowing them to live longer, the sulfamerazine might prove to be more effective.

Whether or not this time relationship between trauma and effectiveness of therapy holds true for human beings is not known. However, it is obviously important that patients with injuries that cause marked crushing of tissues should receive intensive antibacterial therapy as

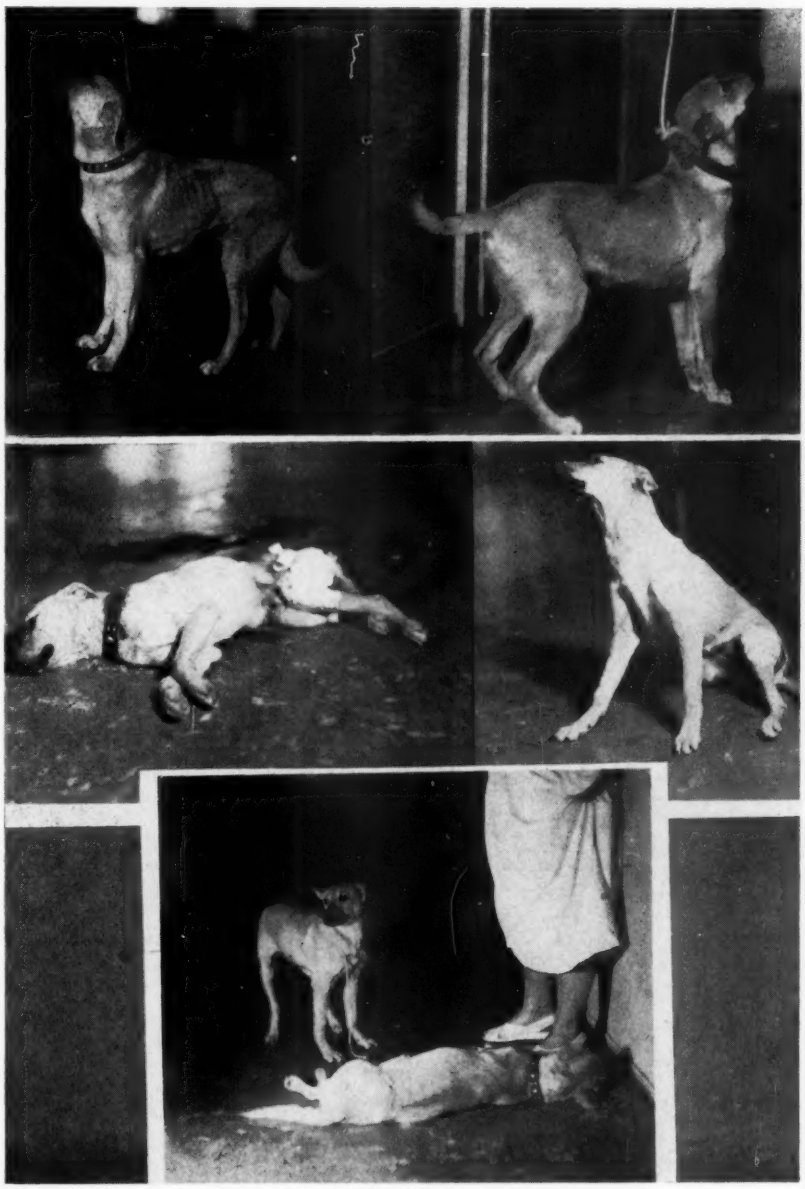
TABLE III

CONCENTRATION OF SULFAMERAZINE IN BLOOD AND TISSUES OF DOGS WITH CRUSHED MUSCLE

EXPERIMENT	DOG NO.	BLOOD (MG. %)	NORMAL MUSCLE (MG. %)*	CRUSHED MUSCLE (MG. %)
Systemic administration of sulfamerazine immediately after trauma	1	14.3	Trace	20.0
	2	6.5	5.5	14.3
	3	6.3	8.7	11.8
	4	---	26.9	29.4
	5	7.9	17.0	58.1
	6	12.3	31.3	50.0
	7	11.7	16.3	65.8
	8	12.5	15.6	107.6
	9	11.6	17.0	113.0
	10	11.6	15.5	48.0
	11	11.6	38.5	65.8
	Mean	9.5	17.5	53.1
Systemic administration of sulfamerazine six hours after trauma	12	13.5	29.4	61.0
	13	15.6	20.2	----
	14	14.3	11.5	100.0
	15	16.7	27.3	161.5
	16	13.2	24.5	17.5
	17	18.6	28.5	57.6
	18	9.2	15.5	----
	19	20.8	40.0	105.5
	Mean	15.2	24.6	83.9
Systemic administration of sulfamerazine seventeen hours after trauma	20	8.5	12.5	39.7
	21	13.2	25.0	55.0
	22	10.8	40.0	25.0
	23	7.4	17.0	48.0
	24	---	47.5	78.4
	Mean	10.0	28.4	49.2
	Total Mean	11.6	23.3	62.1

*Mg. per 100 Gm. dry tissue.

soon as possible. Even though, in our experiment, sulfamerazine proved to be ineffective when administration was delayed for twenty-four hours, nevertheless, the drug should be administered to patients for some possible benefit. In these cases, the use of plasma would appear to be most important since, if the shock can be controlled with plasma, the antibacterial agents may now be effective. It is clear that local



A.

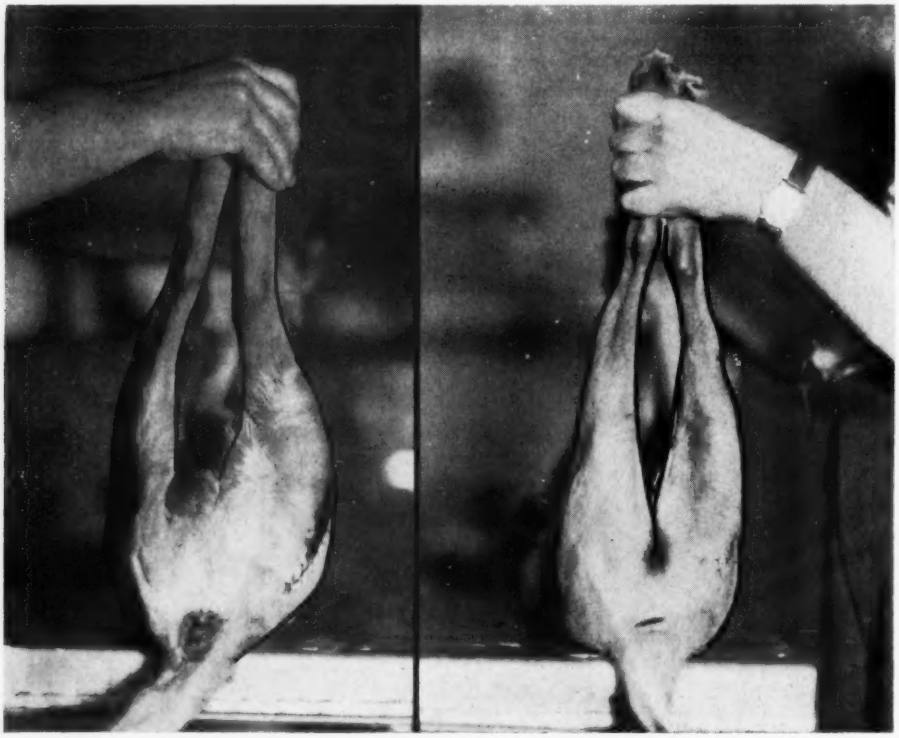
B.

C.

Fig. 1.—Two dogs (*A*) before being subjected to muscle-crushing procedure, and *(B)* twenty-four hours after operation; one dog received sulfamerazine therapy and is in good condition, the other dog received no treatment and is in profound shock. *(C)* Four days after operation, dog which received sulfamerazine is in good condition, and dog which remained untreated is dead.

administration of the drug, while of great benefit, may be insufficient to prevent shock and death, and systemic administration should be employed.

Treatment of toxic shock due to this type of muscle crushing with antibacterial agents continues to be extremely satisfactory. Re-emphasizing the role of bacteria in toxic shock, it is of interest to note that, so far, of fifty dogs which received adequate antibacterial treatment in this and the previous study, none developed shock and all remained in excellent clinical condition, whereas of fifty-two untreated or inadequately treated dogs, fifty developed severe shock and the majority died.



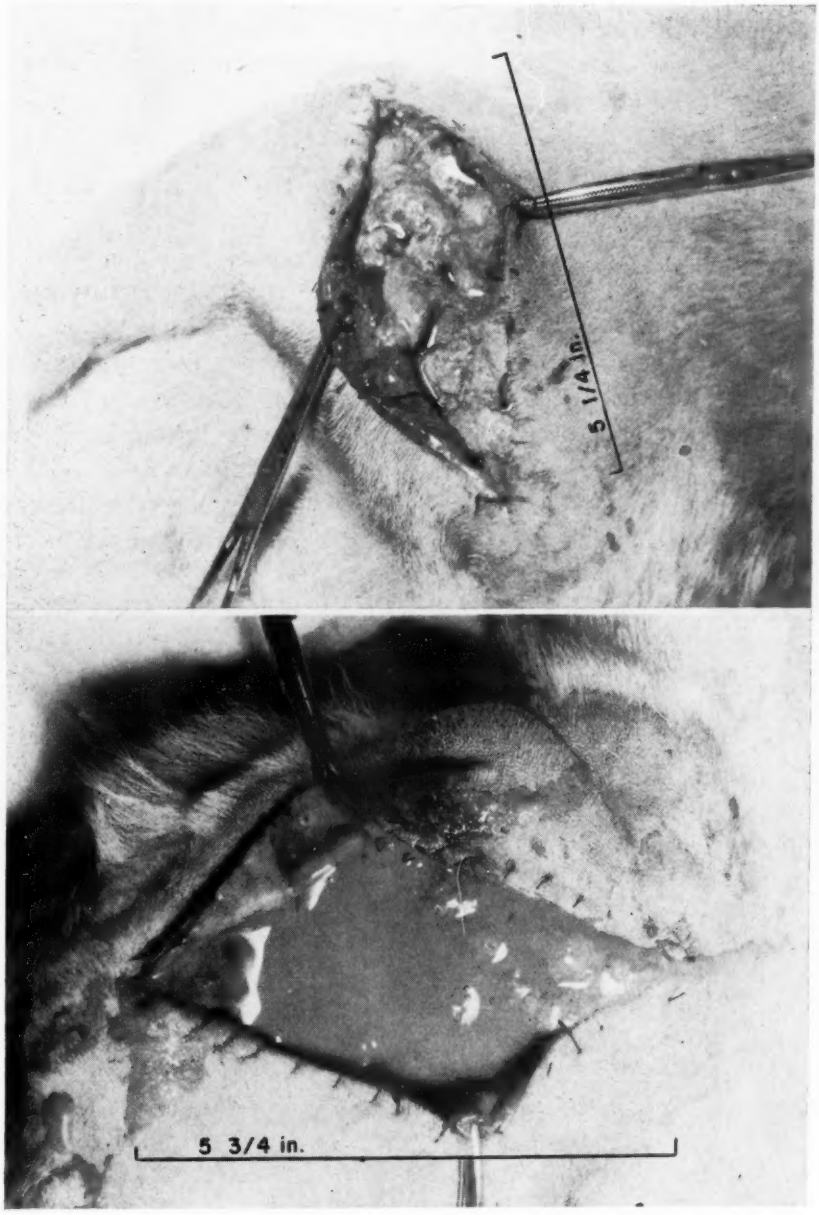
A. *B.*

Fig. 2.—Hindquarters of both animals, demonstrating the difference in size of operated legs. Treated dog (*B*) has only very slight swelling of operated leg. Untreated dog (*A*) has decided swelling of operated quarter, a great deal of which is due to gas.

We wish to mention here that, to us, the clinical appearance of the animals has proved to be the most important diagnostic factor in this type of shock. Fig. 1 shows two dogs (*A*) before being subjected to the muscle crushing procedure, (*B*) twenty-four hours after the operation, and (*C*) on the fourth day after operation. One dog received sulfamerazine therapy and the other dog was untreated. The treated dog remained in good condition except for a slight limp when walking. The untreated animal was in shock twenty-four hours after the operation and was dead on the fourth day. Fig. 2 shows the difference in

size of the operated legs of the two animals. The leg of the treated dog is only slightly swollen and the operated leg of the untreated dog is decidedly swollen, due mainly to gas with a moderate amount of fluid. Fig. 3 shows the wounds of the two animals at autopsy. The wound of the treated dog appears relatively clean and dry although

A.



B.

Fig. 3.—Wounds of the two animals at autopsy. *A*, Wound of animal treated with sulfamerazine appears relatively clean and dry. *B*, Wound of untreated animal shows accumulation of fluid.

the crushed, devitalized muscle is present in large amounts (79.0 Gm. of muscle was crushed in this case, 0.65 per cent of the body weight). The wound of the untreated animal shows the amount of fluid present. The weight of the muscle crushed in this case was 56.0 Gm., 0.41 per cent of the body weight.

The local and systemic use of pencillin in the muscle-crushing type of shock is being investigated at the present time, and the use of sulfamerazine in other types of shock will be presented in future reports. The treatment of animals in shock twenty-four hours after trauma is also being investigated.

CONCLUSIONS

1. Sulfamerazine administered locally partially prevents shock induced by muscle crushing.

2. Systemic administration of sulfamerazine immediately or six hours after operation is completely effective in preventing the occurrence of this type of shock.

3. Systemic administration of sulfamerazine seventeen hours after operation is slightly effective.

4. Systemic administration of sulfamerazine twenty-four hours after operation is ineffective.

5. After systemic administration of sulfamerazine, the ischemic, crushed tissue contains a higher concentration than does the normal muscle of the same animal.

6. If these results are applicable to human beings with crush injuries, treatment should be as follows: Following débridement, sulfamerazine should be administered both locally and systemically and the drug continued for several days in adequate amounts.

7. The role of bacteria in shock due to muscle crushing is re-emphasized, for fifty out of fifty-two untreated or inadequately treated animals developed shock and the majority died, whereas none of fifty dogs adequately treated by antibacterial agents developed shock.

REFERENCES

1. Prinzmetal, M., Freed, S. C., and Kruger, H. E.: Pathogenesis and Treatment of Shock Resulting from Crushing of Muscle, War Med. **5**: 74, 1944.
2. Abraham, E. P., Brown, G. M., Chain, E., Florey, H. W., Gardner, A. D., and Saunders, A. G.: Tissue Autolysis and Shock, Quart. J. Exper. Physiol. **31**: 79, 1941.

THE RETENTION OF INTRAVENOUSLY INFUSED GELATIN

Observations in Man*

Alexander Brunschwig, M.D., and Sabra Nichols, B.S., Chicago, Ill.
(From the Department of Surgery, University of Chicago)

IN RECENT years parenteral injection of nitrogenous nutriment has become feasible by virtue of the development of casein digests suitable for intravenous injection. Evidence has also been presented in support of the view that protein molecules injected intravenously (homologous plasma proteins) might be utilized for nutrition. The use of "complete" foreign proteins would not seem possible in view of their antigenic properties. However, certain samples of gelatin have recently been found suitable for intravenous injection in that no immediate reactions were produced (except in isolated instances and these were not serious), sensitization did not develop, and no late toxic effects were manifested.[1, 2] Gelatin, however, is an incomplete protein in that it lacks a number of the essential amino acids. As the sole source of protein in the diet, it will not permit of normal growth and development of experimental animals.

In view of the tolerance of human patients to repeated intravenous injections of gelatin, and evidence that some of it is metabolized,[2] further studies were carried out in a series of twenty-three patients to determine how much of this material might be excreted in the urine under the usual conditions of intravenous clinical administration. This question is of obvious importance since if most of the injected material is excreted unchanged in the urine, little opportunity for utilization will be afforded and further investigations of gelatin (and possibly other nonantigenic foreign proteins) as an intravenous nutriment will hardly be worth while.

METHODS

Twenty-three patients with various conditions received one or repeated daily intravenous injections of gelatin. In some instances the injections were made in the immediate postoperative period, and the studies carried out when the patient was receiving almost nothing by mouth. In others, the studies were carried out while the patient was partaking of the usual hospital diet. Where one injection was given urine was collected for at least seven days including, of course, the day of injection. Furthermore, urine was collected prior to injection for the control studies which will be discussed. Where several consecutive daily injections were given, urine was collected after cessation of injections until no gelatin could be detected in them.

*This study was facilitated by a grant from the Edible Gelatin Manufacturers Research Society, New York, N. Y.
Received for publication, May 17, 1944.

The gelatin solutions were prepared as follows: Flakes of pigskin gelatin were dissolved in .85 per cent saline solution and autoclaved for thirty minutes at fifteen pounds pressure and 120° C. A precipitate formed which was separated by filtration and discarded. The autoclaving was repeated after adjustment to pH 8 with NaOH; a second precipitate formed and was discarded. The solution was then divided into 400 c.c. bottles and autoclaved a third time. It remained clear in most instances and was light yellow in color. If a precipitate formed, filtration and autoclaving were repeated. Each batch was tested for pyrogenicity in rabbits (U.S.P. procedure) and the samples used only if the test was negative.

According to the manufacturer the viscosity of the gelatin was "less than 20" (plasma is about 18 according to the same scale) and the "plunge number was less than 30."

Gelatin is precipitated by alcohol and not by trichloracetic acid. The method for estimation of gelatin in the urine was as follows:

> Two cubic centimeters of urine were added to 18 c.c. of 5 per cent trichloracetic acid and allowed to stand overnight.
>
> Two cubic centimeters of the same urine sample were added to 18 c.c. of 95 per cent alcohol and allowed to stand overnight.
>
> These were filtered (using Whatman No. 44 paper) and total N. determination (micro-Kjeldahl) were made on 5 c.c. of each filtrate.
>
> The values of the alcohol filtrate were subtracted from the values of the trichloracetic filtrate and the difference regarded as "gelatin N." Conversion into grams of gelatin was made by multiplying the total gelatin N. excreted in each twenty-four hours by the factor 5.55.

To control this method, known quantities of gelatin were added to samples of normal human urine and in three such experiments the data were as follows:

THEORETICAL QUANTITY (KNOWN ADDED GELATIN)	ACTUAL QUANTITY RECOVERED BY METHOD DESCRIBED
6.65 Gm.	6.68 Gm.
7.21 Gm.	7.50 Gm.
21.30 Gm.	21.00 Gm.

Further control studies showed that nine volumes of trichloracetic acid failed to precipitate gelatin from aqueous solution whereas nine volumes of 95 per cent alcohol did afford complete precipitation from aqueous solution.

In a few of the patients, prior to gelatin injections there were differences in total N. determinations between the trichloracetic acid and alcohol filtrates, respectively. Corrections for this were made in the final

estimations of the amount of gelatin in the urines after injection. Such differences were due to nonprotein nitrogenous substances precipitated by the alcohol. Only a small minority of the patients here studied exhibited appreciable quantities of such substances.

In all the patients most of the gelatin recovered in the urine appeared within twenty-four hours after the last injection and it continued to be excreted for the next forty-eight hours in diminishing amounts. The sample of urine collected during the fourth twenty-four-hour period following injection usually did not contain gelatin but collection of urine specimens were continuous until three consecutive twenty-four-hour specimens were obtained in which no gelatin N. was recovered.

DISCUSSION

In Table I the results in patients who received a single injection of 400 to 800 c.c. of gelatin solution are summarized. They fall into two groups: (1) Those in whom appreciable quantities of injected gelatin were not recovered in the urine (eleven patients), and (2) those in whom there was little or no "retention" of gelatin (six patients). The term retention is employed to indicate that portion of gelatin not recovered in the urine. Part of the unrecovered gelatin may have been metabolized and its decomposition products excreted, or it may have been retained as such in the organism possibly to be subsequently metabolized or to be utilized for synthesis of body protein. Previous studies have shown that urea excretion is elevated following intravenous injection of gelatin.[1, 2] That intravenous gelatin might be utilized in synthesis of body protein has not yet been actually demonstrated. Of the patients who retained more than 26.7 per cent, the average was 43.1 per cent of the quantity injected. Among the patients who retained 12.8 per cent

TABLE I

PATIENTS WHO RECEIVED ONE INJECTION OF GELATIN

PATIENT	DIAGNOSIS	GM. GELATIN INJECTED	GM. GELATIN EXCRETED IN URINE	% GELATIN "RETAINED"
1. He.	Carcinoma of colon	26	12.3	52.6
2. Ga.	Inguinal hernia	26	15.6	40.0
3. Bru.	Tuberculous peritonitis	27.9	18.5	33.7
4. Pl.	Peptic ulcer	27.9	14.4	48.3
5. Gop.	Carcinoma of breast	22.7	10.5	53.7
6. Ro.	Carcinoma of rectum	51.6	36.1	30.0
7. St.	Peptic ulcer	56.2	49.4	12.0
8. Fe.	Carcinoma of rectum	65.0	21.8	66.4
9. Co.	Stenosis common bile duct	31.8	15.3	51.8
10. Mc.	Carcinoma of breast	31.8	23.3	26.7
11. Ru.	Carcinoma of colon	67.2	49.0	27.0
12. Ar.	Carcinoma of colon	32.9	18.3	44.3
13. Fi.*	Hyperthyroidism	21.1	20.66	0.0
14. Bro.*	Carcinomatosis	9.75	9.75	0.0
15. Le.	Echinococcus cyst of liver	25.2	21.96	12.8
16. Th.	Cirrhosis liver	25.2	23.05	8.5
17. Hi.*	Cirrhosis liver	26.6	26.6	0.0

*Patient had pyrogenic reaction.

or less there were three who excreted the total amount injected. Each of these exhibited a pyrogenic reaction following the injection and one of the patients had cirrhosis of the liver (Case 17). Of the three who retained small quantities, two had liver disease. It is suggested, therefore, that in primary liver disease there is limited retention of injected gelatin. This might well be anticipated in view of the important role of the liver in protein metabolism. However, in other instances not reported in this study, primary liver disease was sometimes present when there was appreciable retention of injected gelatin.

In Table II are summarized the results in six patients who received several consecutive daily injections. There was appreciable retention in all of them, the average being 40.9 per cent of the gelatin injected. This agrees quite well with the results obtained in studies of single injections where, as stated previously, 43.1 per cent was retained.

TABLE II

PATIENTS WHO RECEIVED SEVERAL DAILY INJECTIONS

PATIENT	DIAGNOSIS	NO. OF DAILY INJECTIONS	GM. OF GELATIN INJECTED	NO. OF DAYS URINE COLLECTED	GM. OF GELATIN EXCRETED	% OF GELATIN "RETAINED"
18. Got.	Carcinomatosis	5	130	13	86.9	33.0
19. Is.	Empyema	8	170.6	14	120.6	28.4
20. Tr.	Carcinoma of colon	5	150	11	86.6	42.4
21. Ha.	Cholecystitis	4	231.7	10	125.8	45.0
22. Di.	Carcinomatosis	8	524.5	10	245.3	53.0
23. Po.	Peptic ulcer	2	130.7	4	74.5	43.0
			Average % retained			40.9+

It is not to be inferred that these studies are regarded as final evidence to justify assumption that intravenous gelatin is a protein food. Evidence for appreciable *utilization* is not yet presented. Emphasis is here placed only on the fact that protein as gelatin may be administered to the organism and that there is retention of appreciable quantities of this substance.

SUMMARY

Evidence is presented to indicate that 40 to 43 per cent of gelatin injected intravenously in man as an 8 per cent solution in physiologic saline is retained in that only 60 to 57 per cent is recovered in the urine. The relative amount of gelatin retained is approximately the same whether one or eight daily injections are made. Thus, gelatin injected intravenously constitutes one method by which nitrogenous material may be administered to the organism.

REFERENCES

1. Brunschwig, A., Scott, V. B., Corbin, N., and Moe, R.: Proc. Soc. Exper. Biol. & Med. 52: 46-48, 1943.
2. Brunschwig, A., Corbin, N., and Johnston, C. D.: Ann. Surg. 118: 1058-1063, 1943.

INTESTINAL OBSTRUCTION

I. The Protective Action of Succinylsulfathiazole Following Simple Venous Occlusion*

Stanley J. Sarnoff, M.D.,† and Edgar J. Poth, M.D., Ph.D.,
Galveston, Texas

(From the Departments of Surgery, The Johns Hopkins University School of Medicine and The University of Texas Medical Branch)

THE problem of intestinal obstructions is an extremely complicated one with a large number of variables which cannot be easily controlled even in carefully planned experiments. The importance of the effects of pressure within the lumen of the bowel, and the blood supply to the involved segment, as well as the types and virulence of organisms which are contained in the gut has long been recognized. It would, therefore, be highly desirable in an experimental study if these various factors could be separated and their individual effects evaluated.

Succinylsulfathiazole[1-4] has been shown to alter the bacterial flora of the intestinal tract in a significant manner both in dogs and human beings. It would be interesting, therefore, to observe whether or not an alteration of the bacterial flora would in any manner change the course following venous occlusion of a segment of bowel.

For the purposes of this experiment, a preparation was made which, while seldom reproduced clinically, is so simplified that it is hoped some of the complicating variables will be eliminated. Simple, complete venous occlusion to a segment of bowel without obstruction of the lumen of the bowel was chosen as the preparation for study. This was accomplished by carefully isolating and doubly ligating all of the veins in the mesentery about halfway between the bowel and the root of the mesentery. Care was taken not to injure the accompanying arteries. At either end of the selected segment the arteries and veins in the mesentery running parallel to the axis of the bowel were carefully isolated, doubly clamped, divided, and ligated. The avascular portion of the mesentery at these points was likewise divided, well down toward the root of the mesentery. When this procedure was carried out on a segment of ileum 50 cm. in length lying immediately proximal to the termination of the antimesentery artery of the terminal ileum, no animals survived more than forty-five hours (see Table I).

*Supported by a grant from Sharp & Dohme, Philadelphia, Pa.

†Fellow in the Department of Surgery, the Johns Hopkins University School of Medicine.

Received for publication, May 8, 1944.

A loop of bowel so treated becomes cyanotic to assume a deep purplish discoloration within thirty minutes. The veins are markedly engorged and the arterial pulsations, which are vigorous at first, become progressively less and finally disappear. The engorged segment of bowel becomes thickened and there is some bleeding into the lumen of the bowel. Beginning at the mesenteric border of the bowel and dissecting downward along the occluded veins to the level of the ligatures, there is extravasation of blood into the mesentery, first noticeable about twenty minutes after the ligatures are applied. Proximal to this point the tissues are normal (Fig. 1). If the segment is exposed to the air, its temperature will have declined to within one degree of the temperature of the room within two and one-half hours.

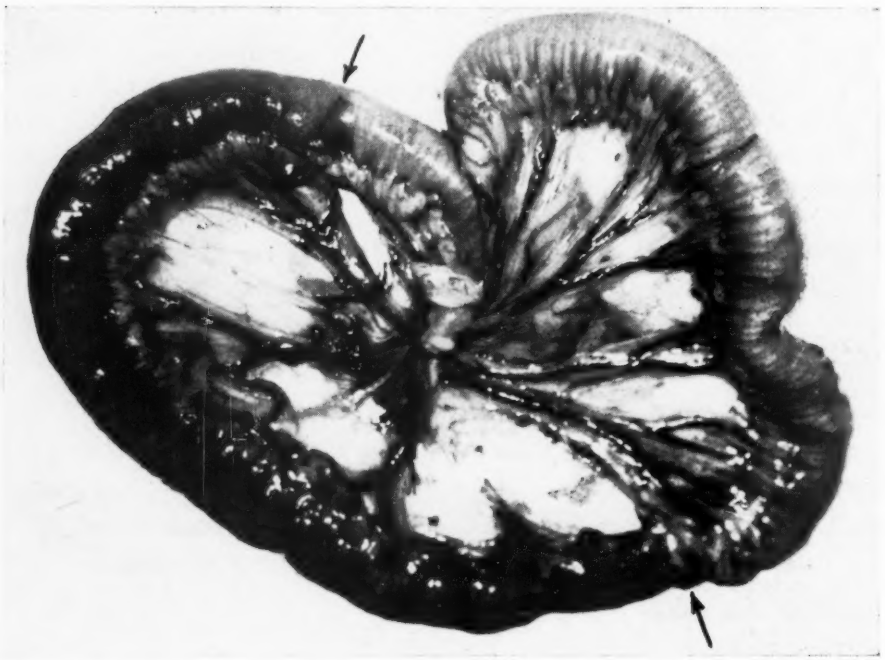


Fig. 1.—A loop of ileum 50 cm. in length is shown twenty minutes after ligation of the veins in the mesentery as well as the artery and vein which run parallel to the axis of the bowel at either end of the segment as indicated by the arrows. The ligatures have been cut long and can be identified. The segment of ileum has become cyanotic and suffused with blood. The veins are distended. The extravasation of blood into the involved mesentery has progressed sufficiently to be visible.

There will be no change of temperature in an adjoining uninvolved segment in the bowel which has been exposed in a similar manner. If at this time the involved segment is cut across, there is practically no bleeding and it is evident that there has been almost complete cessation of blood flow to the segment.

THE EXPERIMENTAL PROCEDURE

Fifteen mongrel dogs were divided into two groups, one of eight controls and one of seven animals which received ½ Gm. per kilogram

TABLE I

DOG	WEIGHT IN KG.	PREOPERATIVE SUCCINYLSULFATHIAZOLE	SURVIVAL TIME (HR.)
1	7.0	Control	12
2	8.0	Control	34
3	7.5	Control	30
4	10.0	Control	35
5	10.0	Control	45
6	10.0	Control	37
7	12.0	Control	37
8	12.5	Control	35
9	6.5	½ Gm./kg. for 10 days in the food	Until sacrificed one mo. P.O.
10	9.0	½ Gm./kg. for 10 days in the food	48
11	6.0	½ Gm./kg. for 10 days in the food	Until sacrificed one mo. P.O.
12	12.0	½ Gm./kg. for 10 days by stomach tube	24
13	11.0	½ Gm./kg. for 10 days by stomach tube	Until sacrificed 50 days P.O.
14	10.0	½ Gm./kg. for 10 days by stomach tube	Until sacrificed 50 days P.O.
15	10.5	½ Gm./kg. for 10 days by stomach tube	Until sacrificed 50 days P.O.

of body weight per day of succinylsulfathiazole for ten days before operation, as indicated in Table I. Bacteriologic studies on the stools of the treated animals showed a significant lowering of the coliform bacteria as reported by Poth, Knotts, Lee, and Inui.[2]

Under ether anesthesia and strict asepsis the veins of segments of ileum 50 cm. in length were ligated as indicated previously. The laparotomy wounds were then carefully closed. For the first forty-eight hours after operation water was given to the animals if they desired to drink, but food was withheld.

During the first twenty-four hours after operation all of the animals appeared extremely ill, and it was impossible to predict which individual dog would survive. The control group of animals ordinarily had bloody stools. This observation was less frequent in animals which had received succinylsulfathiazole therapy.

All of the control animals and two of those receiving preoperative succinylsulfathiazole therapy died during the first forty-eight-hour postoperative period. Immediate autopsy showed all of these animals to have a purulent peritonitis with blood in the peritoneal cavity and a bloody fluid in the intestinal loop. All of the control animals showed gross perforations of the involved segment. The two animals which had been treated with succinylsulfathiazole preoperatively did not show gross perforations of the ileum but at places only the serosa remained intact. The involved segments were purplish-black, gangrenous, and necrotic with large, jagged perforations measuring as much as 5 to 6 cm.

The animals which survived were sacrificed after thirty or fifty days. There were dense adhesions around the involved segment of ileum

which had acquired a striking collateral venous drainage. These veins were of three different sources; the most important ones were those in the omentum and in the previously avascular portion of the mesentery. The third less important venous collateral developed in the adhesions with loops of normal bowel. When these adhesions were separated, considerable bleeding occurred. Otherwise, this segment of bowel could not be distinguished from adjoining loops of ileum. Peristalsis was present and there was no evidence of dilatation or thickening of this portion of the bowel. The only observable change was in the microscopic appearance of the specimens taken after one month at which time there was some fibrosis in the muscularis. After fifty days, however, even these microscopic changes had disappeared and the segments were indistinguishable from normal ileum, except for the presence of adhesions and the atypical venous collaterals.

DISCUSSION

These two groups of experimental animals were subjected to identical operative procedures. One-half of the animals received succinylsulfathiazole for ten days during the preoperative period and again in the postoperative period beginning forty-eight hours after the operation, continuing for a period of two weeks. It is significant that within the first forty-eight hours after operation all the control animals had succumbed. When one considers the appearance of the segment of bowel, both immediately and at the time of the animal's death, it is inconceivable that merely altering the bacterial flora within the bowel would result in survival of the animal and eventual restoration of the involved segment to an essentially normal appearance and physiologic function. The fact that 70 per cent of the treated animals recovered is certainly significant and must indicate the profound effect the drug, succinylsulfathiazole, must have in altering the bacterial flora in the bowel. It cannot, of course, be concluded that the beneficial effects observed from the administration of succinylsulfathiazole are due entirely to the alteration of the bacterial flora. We do not, however, have any pertinent evidence at this time that the difference in behavior of the animals in the two groups is due to anything other than the alteration of the bacterial flora by this drug.

In view of the extensive damage to which these segments of bowel are subjected, it is likely that, if individuals exposed to blast injuries could receive succinylsulfathiazole prior to the trauma, the resulting late perforations would not occur.

These studies are being extended in an attempt to determine the mechanism by which injury occurs in the control animals as well as how this process is altered by the administration of succinylsulfathizole and phthalylsulfathiazole.[5-7]

SUMMARY

The ligation of the venous return from segments of ileum 50 cm. in length is always lethal. When the experimental animals have received therapeutic doses of succinylsulfathiazole, 70 per cent of the treated animals live indefinitely. The immediate and late changes occurring in segments of ileum in treated and untreated animals are described.

REFERENCES

1. Poth, E. J., and Knotts, F. L.: Succinylsulfathiazole, a New Bacteriostatic Agent Locally Active in the Gastrointestinal Tract, Proc. Soc. Exper. Biol. & Med. **48**: 129, 1941.
2. Poth, E. J., Knotts, F. L., Lee, J. T., and Inui, F.: Bacteriostatic Properties of Sulfanilamide and Some of Its Derivatives. I. Succinylsulfathiazole, a New Chemotherapeutic Agent Locally Active in the Gastrointestinal Tract, Arch. Surg. **44**: 187, 1942.
3. Poth, E. J., and Knotts, F. L.: Clinical Use of Succinylsulfathiazole, Arch. Surg. **44**: 208, 1942.
4. Poth, E. J.: Succinylsulfathiazole: An Adjuvant in Surgery of the Large Bowel, J. A. M. A. **120**: 265, 1942.
5. Poth, E. J., and Ross, C. A.: Phthalylsulfathiazole, a New Bacteriostatic Agent, Fed. Proc. **2**: 89, 1943.
6. Poth, E. J., and Ross, C. A.: Bacteriostatic Properties of Sulfanilamide and Some of Its Derivatives: II. Phthalylsulfathiazole, a New Chemotherapeutic Agent Locally Active in the Gastrointestinal Tract, Texas Rep. Biol. & Med. **1**: 345, 1943.
7. Poth, E. J., and Ross, C. A.: The Clinical Use of Phthalylsulfathiazole, J. Lab. & Clin. Med. **29**: 785, 1944.

THE APPLICATION OF SUCCINYLSULFATHIAZOLE AND PHTHALYLSULFATHIAZOLE TO GRANULATION TISSUE: ABSORPTION AND EXCRETION*

EDGAR J. POTH, M.D., PH.D., AND CHARLES A. ROSS, M.S.,
GALVESTON, TEXAS

(From the Department of Surgery, the University of Texas Medical Branch)

THE interesting property of succinylsulfathiazole of poor absorbability from the alimentary tract described by Poth, Knotts, Lee, and Inui in 1942[1] would naturally bring this compound under investigation in a search for a drug suited for topical application without general systemic effects. Although it has been shown that succinylsulfathiazole (Sulfasuxidine) is rapidly absorbed from peritoneal surfaces and from intramuscular and subcutaneous spaces, reports of slight absorption of sulfasuxidine from wounds and granulating surfaces have appeared.[2, 3] Pulvertaft and Mackenzie[2] make the claim from observed data that sulfasuxidine is split to yield sulfathiazole by the action of bacteria and plasma. Poth and Knotts[4] showed that sulfasuxidine is altered to yield a free sulfonamide when suspended in an emulsion of feces at 37° C.

In a recent editorial by Tennison[3] a degree of nonabsorbability of sulfasuxidine from granulating surfaces is claimed which does not conform with our observations. Tennison reports that when as much as 25 Gm. of sulfasuxidine is applied to raw surfaces caused by burns which involved as much as 45 per cent of the body surface there is no measurable absorption of the drug. In order to re-emphasize the limited absorption of sulfasuxidine from the gastrointestinal tract in contradistinction to the rapidity with which the drug is absorbed from subcutaneous and intramuscular spaces and from granulating surfaces this report is submitted.

EXPERIMENTAL OBSERVATIONS ON THE RATE OF ABSORPTION OF SULFASUXIDINE† AND SULFATHALIDINE† FROM GRANULATING SURFACES

Weighed quantities of sulfasuxidine and sulfathalidine[5, 6] were powdered on measured areas of granulating surfaces and covered with either fine meshed, petrolatum gauze or a sheet of thin rubber tissue. Blood specimens were taken at 30-minute, 1-, 2-, 3-, 4-, 8-, 20-, 48- and 72-hour intervals and analyzed for both the free and conjugated forms

*Supported by a grant from Sharp & Dohme, Philadelphia, Pa.

†Sulfasuxidine and Sulfathalidine are proprietary names for succinylsulfathiazole and phthalylsulfathiazole registered by Sharp & Dohme, Philadelphia, Pa.

Received for publication, April 13, 1944.

TABLE I

THE RATE OF ABSORPTION OF SUCCINYLSULFATHIAZOLE AND PHTHALYLSULFATHIAZOLE FROM GRANULATING SURFACES AND THEIR EXCRETION IN THE URINE*

HOUR	CONCENTRATION OF DRUG IN BLOOD MG. PER 100 C.C.		URINARY EXCRETION OF DRUG IN GM.	
	SULFATHIAZOLE	SUCCINYL-SULFATHIAZOLE	SULFATHIAZOLE	SUCCINYL-SULFATHIAZOLE
	10 Gm. Succinylsulfathiazole,† Petrolatum Gauze Bandage			
4	0.0	2.9		
8	0.0	0.0		
12	0.0	0.0		
24	0.0	0.2	0.029‡	4.126‡
48	0.8	0.2	0.059‡	0.232‡
72	1.1	0.0	0.051‡	0.049‡
	Total urinary excretion		0.138	4.407
	Percentage of drug excreted		46.0%	
	10 Gm. Succinylsulfathiazole,† Rubber Bandage			
½	1.3	1.9		
1	0.9	4.1		
2	0.3	5.9		
3	0.9	3.4		
4	0.0	2.8	0.015‡	2.426‡
8	0.3	1.5	0.028‡	1.456‡
24	0.0	0.7	0.016‡	0.410‡
48	–	–	0.000‡	0.052‡
	Total urinary excretion		0.059	4.344
	Percentage of drug excreted		44.3%	
	10 Gm. Phthalylsulfathiazole,§ Rubber Bandage			
½	1.9	3.8		
1½	1.0	10.6		
2½	1.0	13.8		
3½	0.9	5.9		
4			0.009‡	0.463‡
7½	0.3	2.8		
8			0.087‡	2.899‡
24	0.1	0.0	0.044‡	1.324‡
48	0.0	0.2	0.042‡	0.041‡
	Total urinary excretion		0.182	4.727
	Percentage of drug excreted		49.9%	

*Since the succinylsulfathiazole applied to the wound contained 4.22 per cent of sulfathiazole and the phthalylsulfathiazole contained 5.2 per cent of sulfathiazole, it is evident from the relative amounts of free and conjugated compounds excreted in the urine that neither of these drugs is appreciably hydrolyzed either on the surface of the wound or during their passage through the patient. Area of granulations: 870 sq. cm.

†This sample of succinylsulfathiazole contained 4.22 per cent of free sulfathiazole.

‡Quantity of drug excreted in urine for the time interval indicated; that is, first 4 hours, 4 to 8 hours, 8 to 24 hours, etc.

§This sample of phthalylsulfathiazole contained 5.2 per cent of free sulfathiazole.

of the drug. Four-hour specimens of urine were collected for the same period and analyzed for the free and conjugated forms of the compounds. After 72 hours the dressings were removed and leached out with water. The ratio of free to conjugated drug in these washings was determined.

The following is a sample of a characteristic observation:

H. S., a 15-year-old male, had both legs burned eleven months previously. At present the granulating surfaces have a combined area of 870 sq. cm. and represent roughly 10 per cent of the total body surface. On successive weeks 10 Gm. of either sulfasuxidine or sulfathalidine were dusted onto the areas and covered

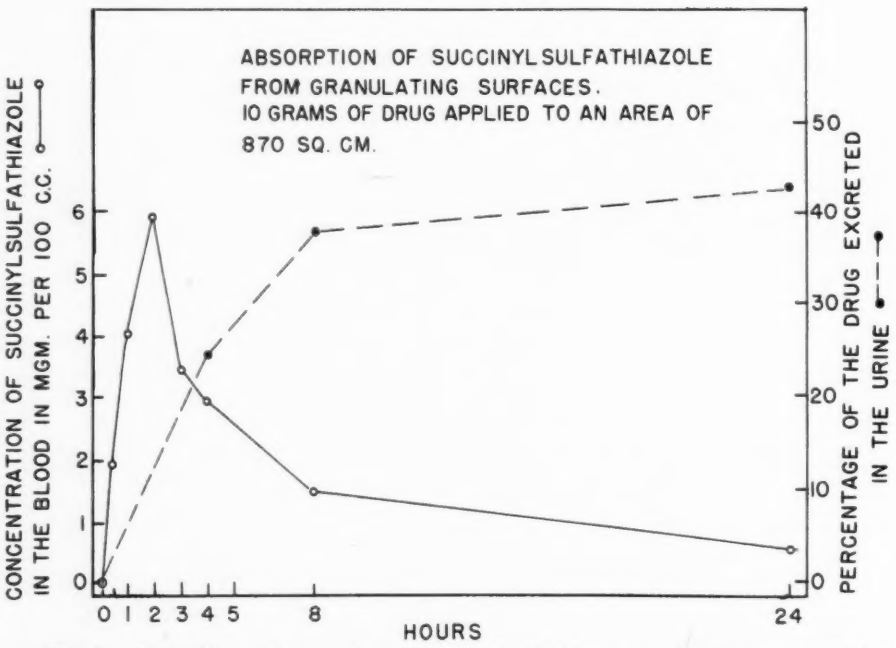

ABSORPTION OF SUCCINYLSULFATHIAZOLE
FROM GRANULATING SURFACES.
10 GRAMS OF DRUG APPLIED TO AN AREA OF
870 SQ. CM.
CONCENTRATION OF SUCCINYLSULFATHIAZOLE
IN THE BLOOD IN MGM. PER 100 C.C.
PERCENTAGE OF THE DRUG EXCRETED
IN THE URINE
HOURS
0 1 2 3 4 5 8 24
0 1 2 3 4 5 6
0 10 20 30 40 50

Fig. 1.—Absorption and excretion of succinylsulfathiazole applied to a granulating surface. The concentration of the drug in the blood is at its maximum in two hours and falls rapidly within eight hours. Thirty-eight per cent of the drug applied to the granulating surface is excreted in the urine within the first eight hours. After this period the concentration of total drug in the blood is insignificant. (See Table I.)

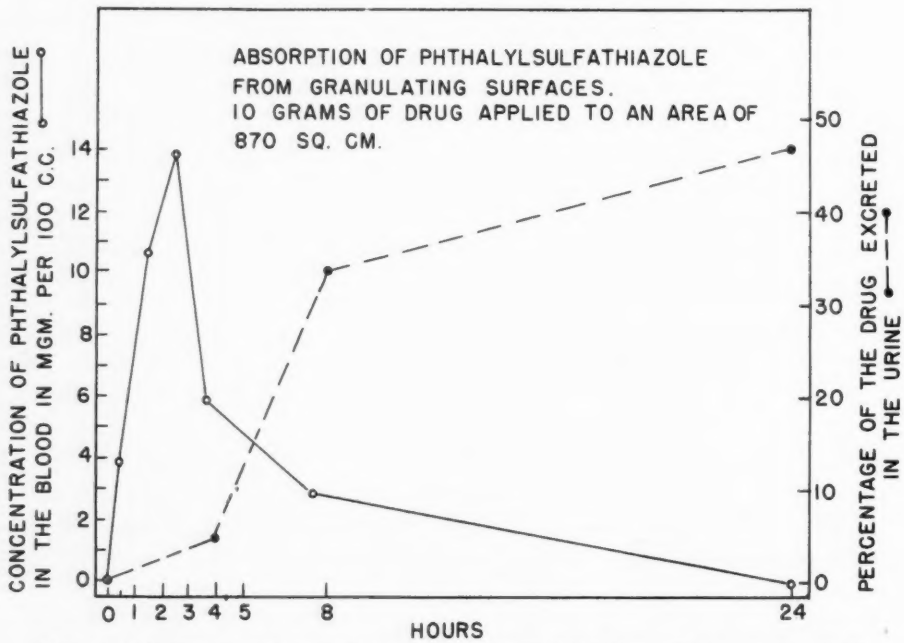

ABSORPTION OF PHTHALYLSULFATHIAZOLE
FROM GRANULATING SURFACES.
10 GRAMS OF DRUG APPLIED TO AN AREA OF
870 SQ. CM.
CONCENTRATION OF PHTHALYLSULFATHIAZOLE
IN THE BLOOD IN MGM. PER 100 C.C.
PERCENTAGE OF THE DRUG EXCRETED
IN THE URINE
HOURS
0 1 2 3 4 5 8 24
0 2 4 6 8 10 12 14
0 10 20 30 40 50

Fig. 2.—Absorption and excretion of phthalylsulfathiazole applied to a granulating surface. The concentration of the drug rises to a surprisingly high level within the first two and one-half hours and drops equally as rapidly thereafter. Thirty-five per cent of the drug applied to the granulating surface is excreted in the urine within the first eight hours. After this interval the concentration of total drug in the blood is insignificant. (See Table I.)

by thin rubber tissue or petrolatum gauze. Specimens were taken as previously described with the results as indicated in Table I and Figs. 1 and 2. Table II shows the observed blood concentrations and the excretion of the drug in the urine when 20 Gm. of succinylsulfathiazole were applied to the same surface daily and in this instance were covered by petrolatum gauze.

The bandages were removed after seventy-two hours and analyzed for residual drug. In the case of the succinylsulfathiazole the analysis showed 0.8 per cent of free drug, while for phthalylsulfathiazole 5.8 per cent of the drug was present as the free compound. These data indicate that the conjugated drugs have not been hydrolyzed on the dressings or while in contact with the granulating surfaces.

TABLE II

THE ABSORPTION OF SUCCINYLSULFATHIAZOLE FROM A GRANULATING SURFACE AND ITS EXCRETION IN THE URINE*

	CONCENTRATION OF DRUG IN BLOOD† MG. PER 100 C.C.		URINARY EXCRETION OF DRUG GM. PER 24 HR.	
DAY	SULFATHIAZOLE	SUCCINYL-SULFATHIAZOLE	SULFATHIAZOLE	SUCCINYL-SULFATHIAZOLE
1	0.9	0	0.046	2.194
2	0.9	0.2	0.077	7.478
3	1.3	0	0.178	3.791
4	0.9	3.8	0.079	5.696
5	0.5	0.2	0.079	4.225
6	1.4	0	0.099	1.713
7	1.3	0	0.083	3.133

*The succinylsulfathiazole applied contained 4.22 per cent of free sulfathiazole. Area of granulations: 870 sq. cm. Daily application: 20 Gm. succinylsulfathiazole.
†Specimens taken 20 hr. after application of drug to the granulating surfaces.

DISCUSSION

These studies demonstrate that succinylsulfathiazole and phthalylsulfathiazole are readily and rapidly absorbed from granulating surfaces although these compounds are but sparingly absorbed through the mucous membrane of the gastrointestinal tract. Roughly 50 per cent of the applied drugs are excreted in the urine within twenty-four hours with the major portion being absorbed from a granulating surface within the initial eight-hour period. After the first twenty-four hours, little drug appears in the urine, because the excess has either soaked into the dressing or has been otherwise carried from contact with the granulations. The low blood concentrations and the rapidity with which these drugs are excreted in the urine re-emphasizes our previous observations on the rapidity with which the compounds are excreted by the kidneys. Observations made on the concentration of the drugs in the blood alone do not indicate the degree and rapidity of absorption of these substances. In order to obtain a correct interpretation of absorption data, it is necessary to supplant such studies by determining the quantities of the free and conjugated forms of a drug excreted in the urine.

There is little reason to expect these compounds to be of great value in the local treatment of infected granulating surfaces. It has been shown that these compounds have but slight in vitro bacteriostatic activity. The ratio of the free and conjugated forms of the drugs excreted in the urine and found as a residue on the dressings indicates that little

of the compounds is split either by the bacteria present on the wounds studied or by the passage of the drugs through the body. Furthermore, since occasional toxic manifestations have been observed even when these compounds are administered orally with only slight absorption, it cannot be assumed with safety that these compounds can be used on granulating surfaces without considerable danger of occasional untoward systemic reactions.

An estimation of the value derived from the topical application of a substance to an infected granulating surface is difficult because of the many uncontrollable factors. We do not feel that any of the sulfonamide drugs can be recommended for topical use in treating infections such as occur on granulating surfaces, due to the fact that there are not sufficient data supporting their value, and the sulfonamides tend to increase scar and keloid formation. Furthermore, it is impossible to control the quantity of drug absorbed, and dangerously high blood levels occur rather frequently. Finally, the patient may become sensitized to the sulfonamide drugs and preclude their future use when the indications are more specific.

CONCLUSION

Both succinylsulfathiazole and phthalylsulfathiazole are rapidly absorbed when applied to granulation tissue. Urinary excretion studies indicate that these drugs are completely absorbed from granulating surfaces within twenty-four hours after application.

It cannot, therefore, be assumed that untoward reactions will not occur following the application of sulfasuxidine or sulfathalidine to granulating wounds, and their topical use is not recommended.

REFERENCES

1. Poth, E. J., Knotts, F. L., Lee, J. T., and Inui, F.: Bacteriostatic Properties of Sulfanilamide and Some of Its Derivatives: I. Succinylsulfathiazole, A New Chemotherapeutic Agent Locally Active in the Gastrointestinal Tract, Arch. Surg. **44**: 187, 1942.
2. Pulvertaft, J. N., and Mackenzie, K. H.: Local Therapy of War Wounds: II. With Sulphasuxidine, Lancet **245**: 379, 1943.
3. Tennison, C. W.: Use of Nonabsorbable Sulfasuxidine in Extensive Burns, SURGERY **15**: 332, 1944.
4. Poth, E. J., and Knotts, F. L.: Clinical Use of Succinylsulfathiazole, Arch. Surg. **44**: 208, 1942.
5. Poth, E. J., and Ross, C. A.: Phthalylsulfathiazole, A New Bacteriostatic Agent, Fed. Proc. **2**: 89, 1943.
6. Poth, E. J., and Ross, C. A.: Bacteriostatic Properties of Sulfanilamide and Some of Its Derivatives: II. Phthalylsulfathiazole, A New Chemotherapeutic Agent Locally Active in the Gastrointestinal Tract, Texas Rep. Biol. & Med. **1**: 345, 1943.

A METHOD FOR THE LOCAL ADMINISTRATION OF PENICILLIN

COLONEL ELLIOTT C. CUTLER AND MAJOR WILLIAM R. SANDUSKY,
MEDICAL CORPS, U. S. ARMY

(From the Professional Services Division, Office of the Chief Surgeon, E.T.O., U. S. Army)

THE purpose of this paper is to report a new method for the local administration of penicillin. The weight and volume of penicillin in relation to the effective dose is exceedingly small. This fact makes essential the use of some diluting substance, or vehicle, if uniform distribution to all parts of the local surface are to be attained.

The usual method of local application and the one used in the majority of instances in a group of casualties treated at U. S. Army station hospitals in the United Kingdom has been to dissolve the sodium salt of penicillin in sterile physiologic saline solution in amounts of 1,000 units per cubic centimeter. This solution is sprayed on the wound by means of an ordinary liquid atomizer. This has proved unsatisfactory because much of the solution runs off the surface and the amount retained in the wound is never accurately known. Many of the possible dry vehicles are undesirable because (1) they react unfavorably with penicillin, (2) they are not absorbable, and (3) they are chemotherapeutic agents themselves. Ointments are equally objectionable, particularly if primary closure of the wound is planned.

To overcome some of these objections we have used dehydrated human plasma as a vehicle for several months.

Under sterile conditions the sodium salt of penicillin is mixed with commercially prepared dehydrated plasma. From 10,000 to 20,000 units of penicillin to 0.2 Gm. of plasma is a desirable proportion; however, this ratio can be varied to fit the particular need. The plasma tends to be lumpy, but gentle stirring reduces it to a light fluffy powder. Penicillin is added, and after gentle stirring, a homogenous mixture is obtained. As plasma is used almost daily in our hospitals, we suggest, to avoid wastage, that the portion of plasma not mixed with the penicillin be used immediately for intravenous therapy.

Uniform distribution of this mixture on the wound surface is accomplished by means of a powder insufflator. A satisfactory inexpensive insufflator can be constructed from standard medical supply items (see Fig. 1).

Received for publication, May 29, 1944.

When sprayed on a wound surface, the penicillin-plasma mixture immediately goes into solution and the tissues assume a yellow color. Complete hemostasis must be attained before insufflation; otherwise the mixture will be washed off at once. We have observed that 0.2 Gm. of plasma is sufficient for fine frosting of a surface 100 sq. cm. in area.

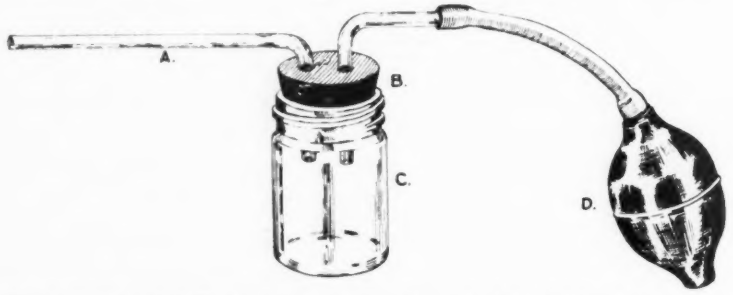


Fig. 1.—A powder insufflator constructed with materials obtained from U. S. Army medical supply items: *A* (44580), 6 mm. glass tubing; *B* (44200), two-hole rubber stopper; *C* (40830), sputum bottle; *D* (77025), rubber bulb hand atomizer.

Laboratory studies show no reduction in potency when penicillin is mixed with plasma. An admixture containing 5 units of penicillin and 0.05 Gm. of plasma was placed in a cylinder on an agar pour plate seeded with 1 c.c. of a twenty-four-hour culture of a test staphylococcus. After overnight incubation a zone of inhibition to bacterial growth 31 mm. in diameter was noted. Another mixture in the same proportion was prepared and refrigerated for ten days. The area of the zone of inhibition was essentially the same.

Experience with this method of local penicillin therapy at a station hospital has demonstrated its superiority over previous methods used. However, the preparation of the mixture as described here is time-consuming and is not practical for general use. Therefore, to obtain a product which can be readily and conveniently used it is suggested that penicillin be dissolved in liquid plasma and the resulting solution be dehydrated and distributed in appropriate sterile containers.

PRIMARY CARCINOMA OF THIRD PORTION OF DUODENUM

THOMAS A. SHALLOW, M.D., SHERMAN A. EGER, M.D., AND JAMES B. CARTY, M.D., PHILADELPHIA, PA.

(From the Samuel D. Gross Surgical Division of the Jefferson Medical College Hospital)

PRIMARY carcinoma of the small intestine is a comparatively rare lesion and extremely so in the third portion of the duodenum. Since an opportunity seldom arises for radical resection of such a lesion, there being only twelve unquestionable cases reported, the following case is described in which a new operative procedure was successfully employed, its advantages discussed, and details of the other resected cases tabulated.

CASE REPORT

History.—A 63-year-old white man was admitted to the Jefferson Medical College Hospital, July 27, 1943, on the medical service of Dr. Hobart A. Reimann. This patient had been in excellent health until one year prior to admission to the hospital, when epigastric fullness occurred about one-half to one hour after meals, and remained for several hours unless relieved by belching. No alkalies were taken. No particular type of food brought on an attack, which occurred every four to six weeks at the onset but gradually increased in frequency and severity. Between attacks he was entirely symptom-free. For two weeks prior to admission epigastric distress and fullness were constant, and were relieved only by vomiting. The vomitus was bile stained and contained particles of food ingested several meals previously but never any blood. Stools diminished in amount but otherwise were normal. There was twenty pounds loss in weight during the last six months, and most of this in the last two weeks. His past medical and family history were negative for ulcer or malignancy.

Physical Examination.—Abnormal findings consisted of mild dehydration, moderate epigastric distention, and a deep, firm, fixed, nontender mass two inches in diameter just above the umbilicus.

Laboratory Data.—The blood count showed hemoglobin 73 per cent, red cells 3,430,000, color index 1.07, and white cells 5,600 with a normal differential.

The gastric contents contained a residual total acidity of 25 and free hydrochloric acid of 20; after a test meal these figures gradually rose to a maximum of 48 and 27, respectively, in the sixth specimen. There was bile present in all the specimens, but blood and lactic acid were absent.

Urine examination was normal. The Wassermann and Kahn reactions of the blood serum were negative. The sedimentation rate was 24 mm. in one hour.

Roentgenographic study of the gastrointestinal tract (by Dr. Paul C. Swenson) showed almost complete obstruction at the beginning of the ascending loop of the duodenum. Flash roentgenograms (Figs. 1 and 2) did not demonstrate the outline of the tumor because the associated spasm and reverse peristalsis instantly returned the barium to the second portion. A re-examination following a period of gastric lavages revealed better tone to the stomach wall and less dilatation. There was again almost complete obstruction at the beginning of the ascending loop of the duodenum, behind which the barium puddled and the duodenum was dilated. Enough

Received for publication, June 3, 1944.

Fig. 1.—Roentgenogram following barium meal showing obstruction in the third portion of the duodenum.

Fig. 2.—Roentgenogram twenty-four hours following barium meal demonstrating the gastric and duodenal retention.

barium could not be forced through the constriction at any time to allow for good contours. The diagnosis made was a lesion in the third portion of the duodenum, probably due to a malignancy, either primary or secondary.

Operation.—After the patient was transferred to the surgical service operation was performed Aug. 4, 1943. The abdomen was opened through an upper right

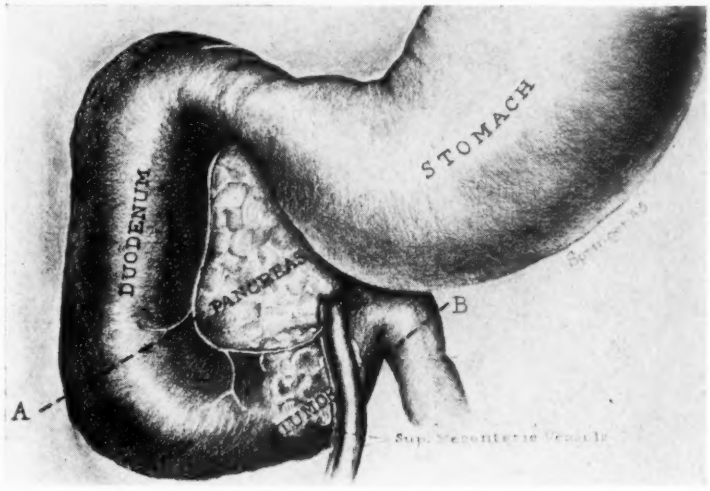


Fig. 3.—Anatomic relationship of tumor represented diagrammatically. Lines *A* and *B* are sites of resection.

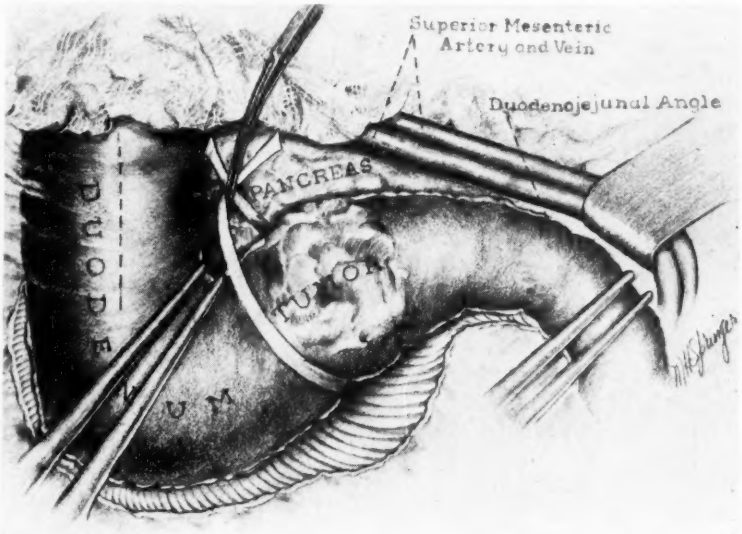


Fig. 4.—Third portion of duodenum and duodenojejunal angle mobilized prior to resection. Dotted line on second portion of duodenum represents site for side-to-side duodenojejunostomy.

rectus incision under spinal anesthesia. A tumor was found involving the postero-superior wall of the third portion of the duodenum beneath the superior mesenteric vessels (Fig. 3). The adjacent retroperitoneal tissue was indurated, but there was no evidence of extension of the growth or metastasis. The entire third portion of the duodenum was mobilized and resected (Fig. 4). The free ends of the bowel

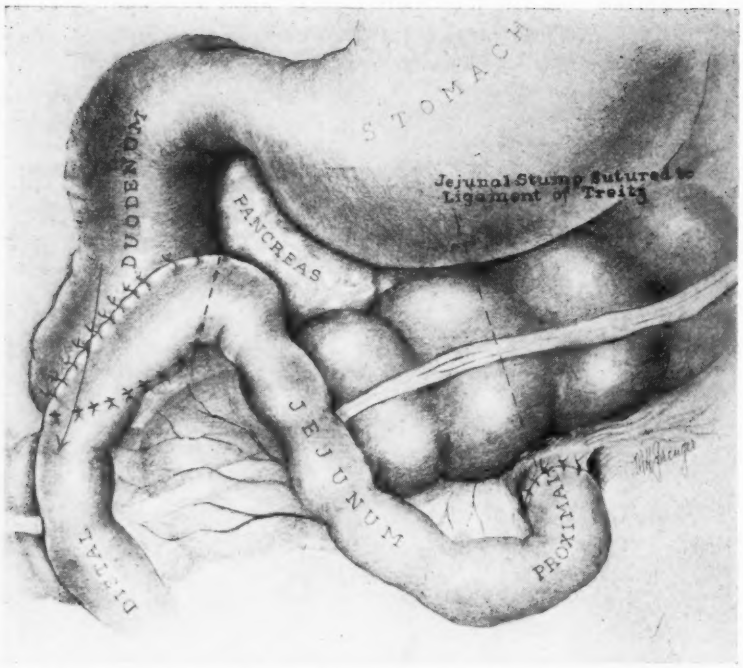


Fig. 5.—Side-to-side antecolic duodenojejunostomy completed. Proximal jejunal stump anchored to ligament of Treitz.

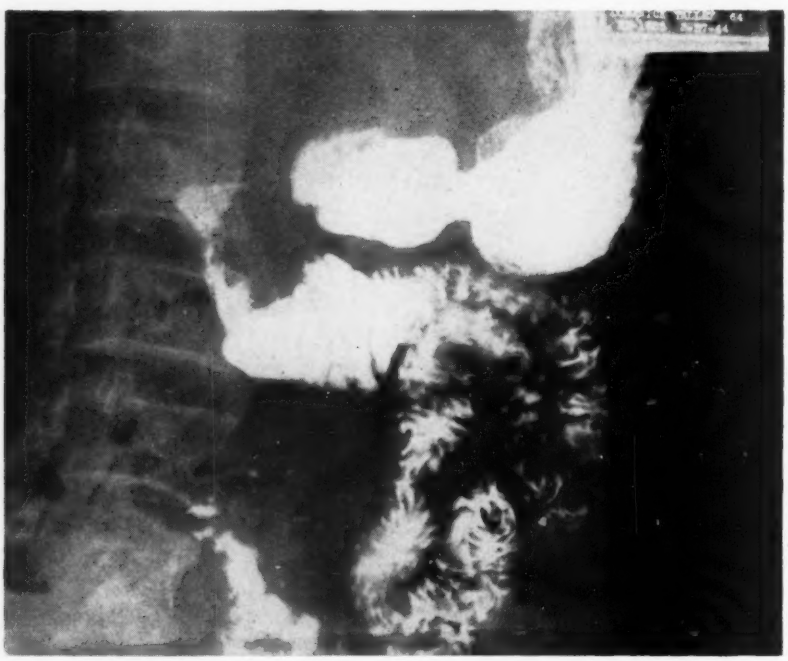


Fig. 6.—Roentgenogram following barium meal, 8 months postoperatively, revealing normal size of stomach and duodenojejunostomy functioning well.

were closed. An antecolic duodenojejunostomy (Fig. 5) was performed in a side-to-side manner anastomosing the jejunum, about ten inches from the ligament of Treitz, to the second portion of the duodenum, just distal to the ampulla of Vater. The suture line of the closed duodenal stump was reinforced by anchoring it to the posterior surface of the jejunum just distal to the anastomosis. The jejunal stump was reattached to the ligament of Treitz leaving the proximal jejunum available for a gastroenterostomy should the duodenojejunostomy stoma have proved inadequate. The abdomen was closed without drainage. The operating time was one hour and fifty minutes. The patient was discharged from the hospital Sept. 18, 1943.

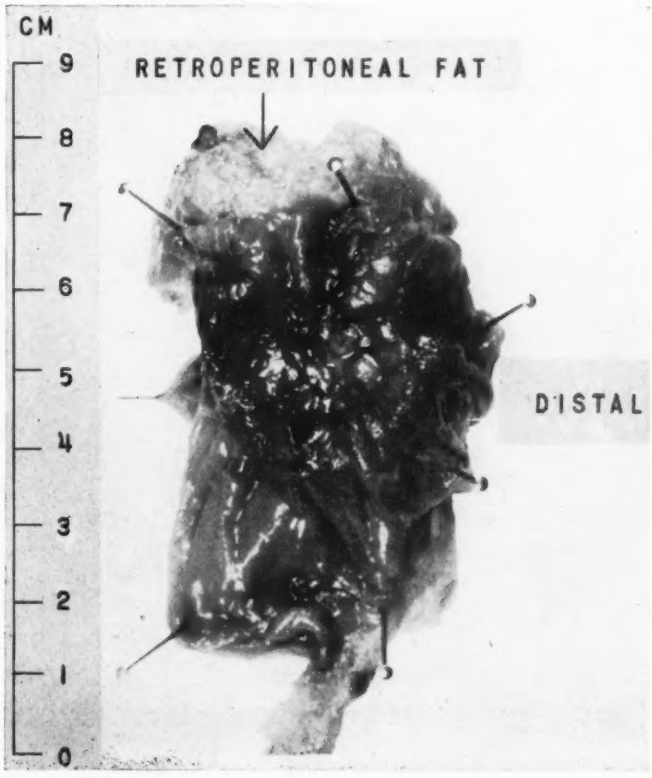


Fig. 7.—Opened specimen of ulcerative adenocarcinoma of third portion of the duodenum.

Pathologic Report.—The removed segment of duodenum contained a central penetrating ulcer 2 cm. in diameter (Fig. 7). In sections through the ulcer base, the epithelium was irregular and nonsecreting, arranged in small cords and acini (Fig. 8). The cells showed marked hyperchromatism and a few mitotic figures. They infiltrated the entire submuscularis mucosa, submucosa, and a portion of the muscle layers. The supporting connective tissue was very scant, containing some plasma cells and lymphocytes. The diagnosis was primary ulcerative adenocarcinoma of the duodenum.

Follow-Up.—At the present time (nine months after operation) the patient is symptom-free, has gained thirty pounds in weight, and x-ray examination following a barium meal reveals no abnormality (Fig. 6).

We have been able to collect from the world literature reports of only twelve unquestionable cases of primary carcinoma of the third por-

tion of the duodenum in which resection was done. The third or inferior portion consists of both the horizontal and ascending segments, terminating at the duodenojejunal flexure. The cases reported by Allen,[1] Mallory,[11] Markus,[12] and Muller[13] are omitted because the growth was either not primary in the third portion of the duodenum or questionable as to its location.

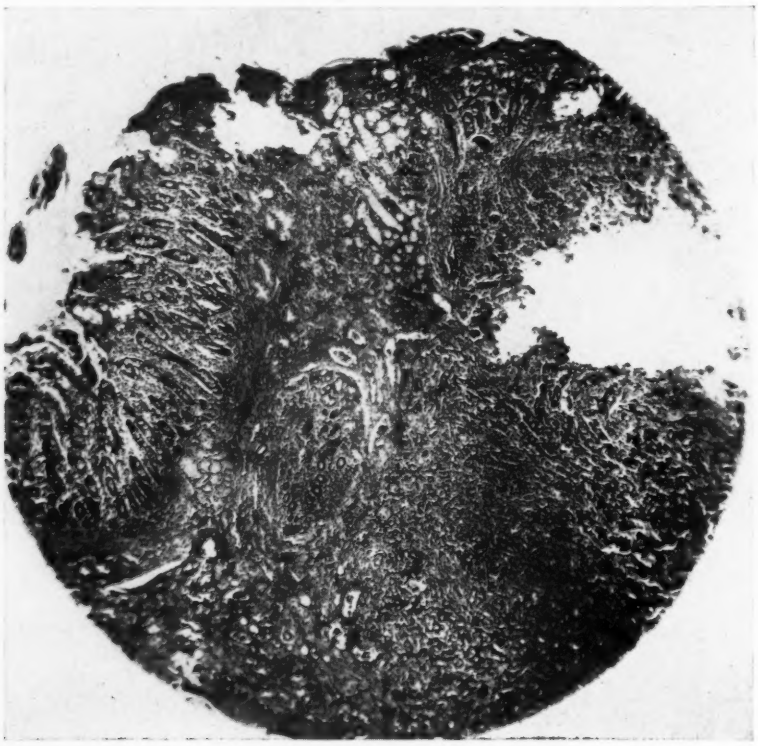


Fig. 8.—Photomicrograph of section through ulcer base of tumor (×37.5).

In Table I are listed the twelve collected cases and our case. It will be noted that there are five end-to-end anastomoses, three side-to-side, two end-to-side, one side-to-end, and one complete duodenectomy. The jejunum was stated to have been brought through the transverse mesocolon posterior to the superior mesenteric vessels in two cases and anterior in one. Two complementary gastroenterostomies were performed, one preliminary to a complete duodenectomy and the other in addition to an end-to-side duodenojejunostomy. The operative mortality was 17 per cent.

In our case a different operation was employed in which an antecolic side-to-side duodenojejunostomy was performed leaving a proximal jejunal loop. This procedure (Fig. 5) has the following advantages:

1. The anastomosis is safer for it is performed where the duodenum has a peritoneal covering.

TABLE I

RESECTED CASES OF PRIMARY CARCINOMA OF THIRD PORTION OF DUODENUM

AUTHOR	PATIENT'S AGE (YRS.)	SEX	LOCATION OF TUMOR TO SUPERIOR MESENTERIC VESSELS	SIZE OF TUMOR (CM.)	OPERATIVE PROCEDURE AND TYPE OF DUODENOJEJUNOSTOMY	RESULTS
Syme[15]	40	M	Posterior	3.2	End-to-end	Well 3 mo. later
Davis[4]	46	F	Distal	4	End-to-end	Died 7 days later
Harries and Harrison[9]	49	F	Distal	1.5	End-to-end	Died 3 mo. later
Bergendal[2]	60	F	Distal	3.5	End-to-end	Well 20 mo. later
Graham[7]	54	F	Proximal	3	End-to-end (jejunum brought posterior to superior mesenteric vessels)	Died 3 mo. later
Lundberg[10]	64	M	Distal	1	End-to-side (jejunum brought posterior to superior mesenteric vessels)	Well 3 mo. later
Tatlow[16]	53	M	Distal	3	End-to-side (also used proximal jejunum for posterior vertical gastrojejunostomy)	Well 4 mo. later
Eger[5]	50	F	Proximal	2.5	Side-to-side (retrocolic)	Died 6 yr. later
Handfield-Jones[8]	54	F	Posterior	1.5	Side-to-side (jejunum brought anterior to superior mesenteric vessels)	Well 16 mo. later
Pauchet and Luquet[14]	61	F	Distal	1	Side-to-end	Well 1 yr. later
Claiborn and Dobbs[3]	47	M	Distal, first operation; also proximal, second operation	5	First stage, gastrojejunostomy; second stage (1 mo. later), complete duodenal resection and cholecystogastrostomy	Died 18 hr. later
Farinas Mayo[6]	50	F	Distal	4	Not stated	Not stated
Shallow, Eger and Carty	63	M	Posterior	2	Side-to-side (antecolic, 10 in. from ligament of Treitz)	Well 9 mo. later
	Extremes, 40-64 Average, 56	M 5 F 8	Distal 8 Proximal 2 Posterior 3	Ave. size 3	End-to-end 5 End-to-side 2 Side-to-side 3 Side-to-end 1 Complete duodenectomy 1 Complimentary gastroenterostomy 2 Not stated 1	Operative mortality 17%

2. The closed duodenal stump is reinforced by being buried in the undersurface of the distal jejunal loop.

3. With the anastomosis side-to-side the angles can be well fortified and the size of the stoma regulated without encroaching on the common bile duct, ampulla of Vater, or the blood supply of the remaining duodenum.

4. With the jejunum antecolic, obstruction from pressure by the superior mesenteric vessels and from the passage through the transverse mesocolon is avoided.

5. A proximal jejunal loop is provided for a gastrojejunostomy should the duodenojejunostomy stoma be inadequate.

SUMMARY AND CONCLUSIONS

A new operation is described and illustrated for re-establishing bowel continuity following resection of the third portion of the duodenum for primary carcinoma and its advantages are enumerated. We believe this method to be safer, simpler, and less time-consuming than those previously reported.

REFERENCES

1. Allen, C. I.: Primary Carcinoma of the Duodenum With Report of 11 Cases, Am. J. Surg. **40**: 89-101, 1938.
2. Bergendal, A.: A Contribution to the Knowledge of Primary Duodenal Cancer, Acta Radiol. **20**: 417-426, 1939.
3. Claiborn, L. N., and Dobbs, W. G. H.: Carcinoma of the Third Segment of Duodenum; Report of Case, SURGERY **4**: 97-102, 1938.
4. Davis, C. R.: Carcinoma of Duodenum; Case Report; Am. J. Cancer **23**: 337-338, 1935.
5. Eger, S. A.: Primary Malignant Disease of the Duodenum, Arch. Surg. **27**: 1087-1108, 1933.
6. Farinas Mayo, L.: Carcinoma del Ángulo Duodeno-yeyunal, Bol. Liga contra el cáncer **9**: 210-214, 1934.
7. Graham, R. R.: Personal Communication; and Carcinoma of the Duodenum: in Operative Surgery, Ed. by Bancroft, F. W., New York, 1941, D. Appleton-Century Co., Inc., pp. 641-643.
8. Handfield-Jones, R. M.: Intrinsic Carcinoma of the Duodenum With Report of Successful Removal, Lancet **2**: 1168-1170, 1938.
9. Harries, D. J., and Harrison, C. V.: Primary Carcinoma of the Small intestine, Brit. M. J. **1**: 923-924, 1935.
10. Lundberg, S.: Cancer of the Duodeno-jejunal Flexure, Acta chir. Scandinav. **56**: 417-424, 1924.
11. Mallory, T. B.: Case Records of the Mass. General Hospital, Case 24162, The New England J. Med. **218**: 687-689, 1938.
12. Markus, H.: Magen-duodenaladenomatose mit Maligner Degeneration des Duodenaladenoms, Klin. Wchnschr. **12**: 617-618, 1933.
13. Muller, J., quoted by Marchand, L., and Guibert, H. L.: Contribution à l'étude de la Lymphogranulomatose Duodénale. Les Possibilities Anatomiques d'Exérèse de la 3e Portion du Duodénum; Ann. d'anat. path. **16**: 311-325, 1939.
14. Pauchet, V., and Luquet: Cancer de la Quatrième Portion du Duodénum, Bull. Acad. de méd., Paris **97**: 276-279, 1927.
15. Syme, G. A.: Carcinoma of the Duodenum; Resection, Recovery, Lancet **1**: 148, 1904.
16. Tatlow, E. T.: Three Consecutive Cases of Carcinoma of the Jejunum, Lancet **1**: 991, 1912.

SPONTANEOUS VENTRAL HERNIA

Report of a Case

Edward Woliver, M.D., and Charles M. Scott, M.D.
Cincinnati, Ohio
(From the Department of Surgery, College of Medicine, University of Cincinnati, and the Cincinnati General Hospital)

VENTRAL hernias are protrusions of the abdominal viscera through the anterolateral abdominal wall occurring at points other than the inguinal, femoral, and umbilical openings. They may be of traumatic (including postoperative) or spontaneous origin. Those of spontaneous origin are less common and may arise in the linea alba, lumbar region, and semilunar line (Spiegel's hernia). Recently Zimmerman and co-workers[1] have suggested another type of spontaneous ventral hernia, produced by a "banding" of the fibers of the internal oblique and transversalis muscles. This paper is concerned with the latter type of hernia and a case recently encountered is reported.

CASE REPORT

H. G. (No. 193246), a 54-year-old white, married, nulliparous female, was admitted to the Cincinnati General Hospital April 30, 1944, with a history of intermittent left lower abdominal pain for several years, with increasing constipation for over a year. On April 23, she had an attack of left lower abdominal pain relieved by catharsis. On April 27, the pain recurred but was not relieved by a cathartic. She began to have severe cramping pains on the left side which spread over the entire abdomen. In addition, she noted the presence of a mass in the left lower abdomen which had appeared, likewise, during previous attacks of pain. There was no history of loss of weight, abnormal stools, or digestive difficulties. The remainder of the history was negative except for a persistent skin rash over the right arm. On admission the temperature was 100.4° F.; pulse, 88; respirations, 20; and blood pressure, 170/100. The white blood count was 14,500; hemoglobin, 14.5 Gm. per cent; and urine, negative. Examination revealed an obese, acutely ill, white female lying flat in bed but becoming very restless during paroxyms of pain. Positive findings were limited to the abdomen which was very obese, distended, and diffusely tender. There was an ill-defined tender mass in the left lower quadrant measuring about 10 cm. in diameter. Peristalsis was audible, synchronous with pain; however, the abdomen was quiet between paroxysms. No impulse on coughing could be felt over the inguinal and femoral rings.

The patient was given nothing by mouth and received an enema which was not productive of feces or flatus. Parenteral fluids were administered. X-rays of the abdomen were interpreted as exhibiting paralytic ileus. The proctoscopic examination and barium enema were negative. Morphine, gr. ¼, was given prior to these examinations, and on the patient's return to the ward from the x-ray department her abdomen was much more relaxed. On further examination it became apparent that the mass was within the abdominal wall. It was believed that the patient had an incarcerated hernia which was interparietal. The patient had been under continuous observation for twelve hours, and it was only through this continued observation that the diagnosis of hernia was established. At operation an interparietal hernia was found lying between the external and internal oblique muscles and containing incarcerated omentum. The neck of the sac was

Received for publication, July 28, 1944.

located just above and lateral to the internal inguinal ring in a defect of the internal oblique and transversalis muscles. The adhesions between the omentum and sac were freed. The omentum was reduced, the sac was ligated as high as possible, and the excess portion excised. The wound was closed in layers with silk, imbricating the external oblique aponeurosis in two layers. The postoperative course was uneventful and the patient was discharged on the seventeenth postoperative day.

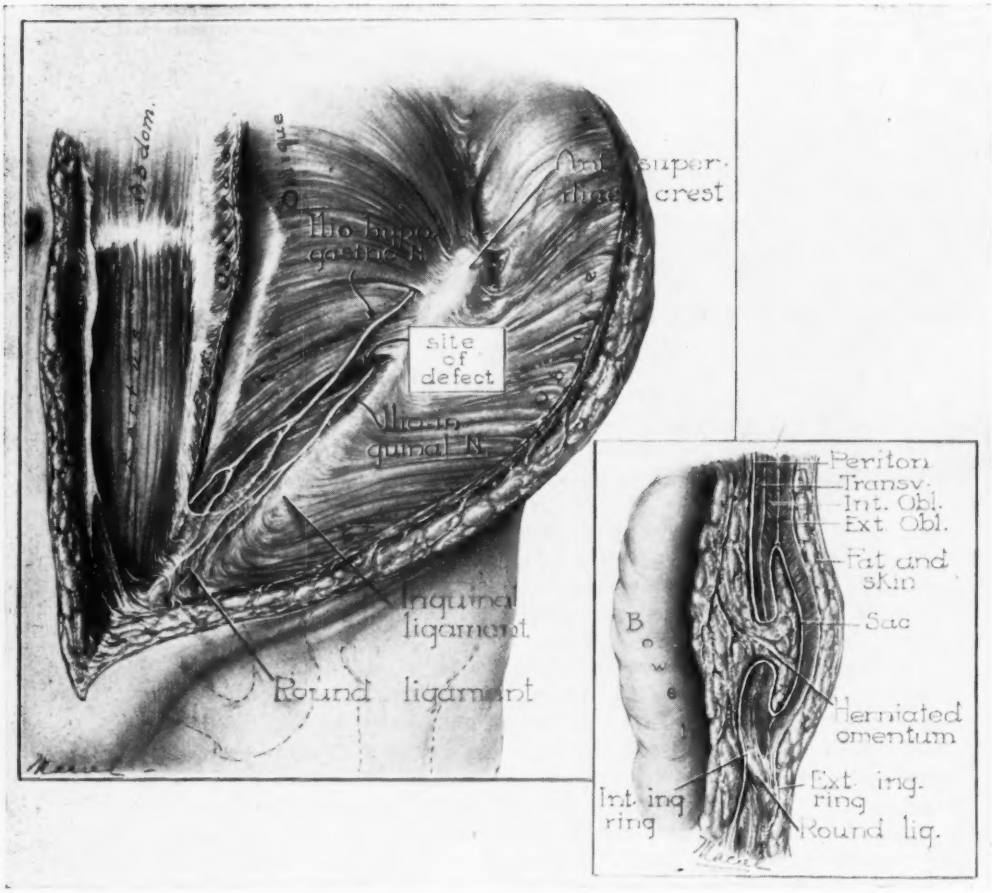


Fig. 1.—Diagrammatic sketch illustrating site of defect and position of hernia sac.

DISCUSSION

A confusion of classification has been found to exist among the group of ventral hernias. Interstitial hernias arising from defects above and lateral to the internal inguinal ring (as in the reported case) have been included previously in the group of interparietal inguinal hernias. Lower and Hicken,[2] in 1931, discussed the interparietal hernias of the inguinal region and presented two case reports. In each instance the sac did not communicate with the internal ring but arose from a defect above and lateral to the internal ring. Kronlein,[3] in 1876, referred to such a case as a "parainguinal interstitial hernia." It is our impression that such hernias differ from the group of true interparietal hernias and are more correctly classified as spontaneous ventral hernias.

Other differences exist between the two types. The sac of the true interparietal hernia is frequently multilocular, whereas in the spontaneous lateral ventral hernia the sac is usually unilocular. The former type of hernia is more frequent in the male, often being associated with an undescended testicle. This is not true of the latter type of hernia. Both types of hernias are similar in that the sac is located between the parietes, the contents frequently being incarcerated and strangulated. The diagnosis is, as a rule, difficult, and may be deferred until determined at the operating or autopsy room. Clinically the patient may complain of abdominal pain associated with an abdominal mass. In an obese patient it may be difficult to determine whether the mass is intraperitoneal or within the abdominal wall. There may be findings suggestive of intestinal obstruction requiring diagnostic sigmoidoscopic and barium enema studies. Incarcerated and strangulated omentum or bowel frequently are found in the sac. Other hernias may also be present. Zimmerman and associates[1] have recently presented a new concept concerning the pathogenesis of this type of hernia, reporting three such cases encountered at operation. They stressed the importance of the occurrence of defects due to banding of the transversalis and internal oblique muscles. These authors studied 500 body halves and discovered deficiencies which could permit of parietal herniation in 109 (21.8 per cent). These deficiencies consisted of slitlike gaps between divergent bundles of fiber. In some instances actual preperitoneal fat herniations were present. An additional congenital anatomic predisposition to hernia was suggested to us in our case. Fig. 1 illustrates how the ilioinguinal nerve emerged through the internal oblique muscle at the lateral angle of the defect. Examination of several cadavers revealed that this nerve, the iliohypogastric nerve, and the deep circumflex iliac artery perforate the internal oblique muscle at the site where such hernias usually occur and may predispose to the weakness.

The treatment, once the diagnosis has been established, is surgical. The interparietal position of the mass may confuse the operator until the external oblique aponeurosis is opened. The contents of the sac should be reduced or resected as is indicated and the sac ligated as high as possible. The parietal defect may be closed with sutures and the repair reinforced by imbricating the external oblique aponeurosis over the site of the defect.

SUMMARY

A case of spontaneous ventral hernia is reported. The etiological and clinical characteristics of this type of hernia are discussed.

REFERENCES

1. Zimmerman, L. M., Anson, B. J., Morgan, E. H., and McVay, C. B.: Surg., Gynec. & Obst. **78**: 535-540, 1944.
2. Lower, W. E., and Hicken, N. F.: Ann. Surg. **94**: 1070-1087, 1931.
3. Kronlein, R. V.: Arch. f. Klin. Chir. **19**: 408-420, 1876.

CONGENITAL EVENTRATION AT THE UMBILICUS

ALFRED H. IASON, M.D.,* BROOKLYN, N. Y.

DEFINITION

THE condition which is usually denominated a "congenital umbilical hernia," is an eventration contiguous to, or in, the umbilicus. About 300 years ago F. Rysch (*Observationum anatomico-chirurgicarum*, 1691) was the first to point out that "no hernia can be called umbilical before the umbilicus exists." The hernial contents were never in the abdominal cavity; they remained outside from the beginning of embryonal life and, consequently, prevented the formation of an umbilicus.

SYNONYMS

The protrusive malformation at the umbilicus has been variously named congenital umbilical hernia, exomphalocele, omphalocele congenitalis, hernia funiculi umbilicalis, ectopia viscerum, amniotic hernia, or amniotic umbilicus.

INCIDENCE

The congenital condition has an equal incidence in the sexes. It occurs in about one birth in 10,000.

A complete exomphalos is one in which the physiologic hernia into the celomic root of the umbilical cord, owing to the failure of closure of the ventral abdominal wall, persists until birth or shortly thereafter. (When only the abdominal wall is involved, the condition is termed gastroschisis completa.)

PATHOLOGIC ANATOMY

The dilated root of the cord serves as the hernial sac (there is no true sac) which appears as a translucent membrane; the "neck" of this sac is encompassed by true skin definitely outlined, and the "fundus" is covered by the irregular network of blood vessels which combine to form the umbilical cord. (Cruveilhier first pointed out that a congenital umbilical hernia is characterized by the absence of a peritoneal sac.)

A disproportion in size between the viscera and the abdominal cavity may result in the condition where a viscus or viscera may remain extra-abdominal and at the base of the umbilical cord. The deciding factor is usually a failure of proper development of the abdominal wall. (See Fig. 1.)

*Attending Surgeon, Adelphi Hospital; Director of Surgery, Brooklyn Home for the Aged.

Received for publication, April 12, 1944.

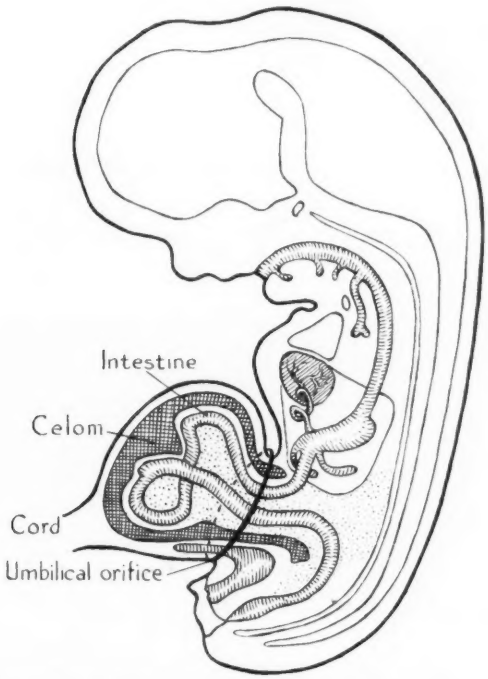


Fig. 1.—Seventeen millimeter human embryo, illustrating the position of the celomic cavity in the wide base of the umbilical cord.

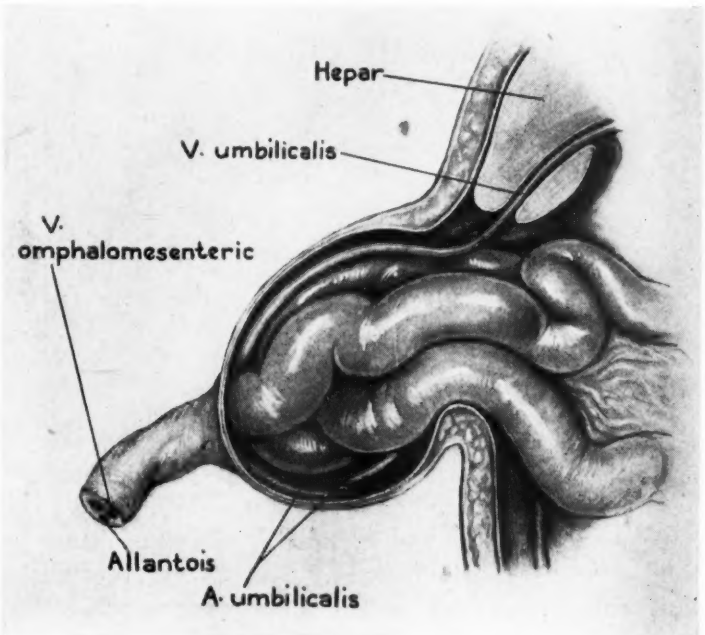


Fig. 2.—Congenital umbilical (cord) hernia, demonstrating contents and vessels.

A congenital defect remains at the umbilicus, either when the midgut fails to return to the abdominal cavity in the tenth week of intrauterine life, or when, though it has returned, the extracelomic pouch of peritoneum fails to close. The failure may be of any degree. (See Fig. 2.)

In some cases the protrusion is ruptured during delivery and the infant is born eviscerated. When this does not occur, the abdominal wall appears to be replaced by a grayish translucent dome and the viscera can be seen through it, the cord being attached to the summit.

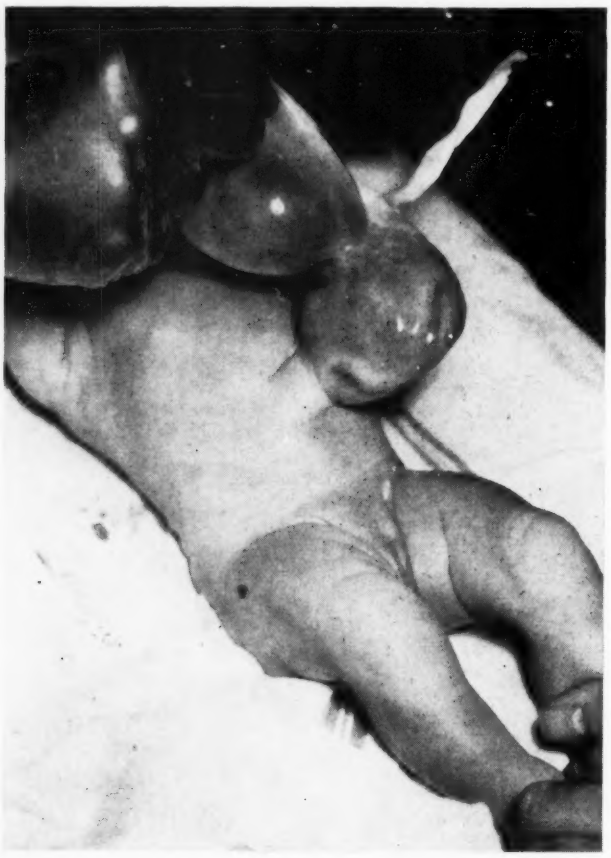


Fig. 3.—Child 1 hr. old with congenital hernia into cord.

The displaced abdominal wall is to be found in the flanks contiguous to the protrusion. The junction between the abdomen proper and the exomphalic mass is distinctive in that there is an abrupt transition from pink skin to Wharton's jelly. The coverings of the mass are amnion, Wharton's jelly, and extracelomic peritoneum. (See Fig. 3.)

The sac is usually about 7 cm. in diameter, but may be as small as 2 cm., and the defect in the fascia varies from 5 to 8 cm. in diameter. The contents are small intestine and proximal colon with the addition,

in many instances, of the greater part of the liver and stomach and pelvic colon. Associated anomalies may be present, such as harelip, undescended testes, and clubfeet.

SYMPTOMS

A newborn infant with a complete exomphalos survives only a few hours. What is immediately obvious is the fact that the navel or umbilical cord is absent and in place thereof is a wide, central, funnel-shaped defect which is covered by translucent tissue of grayish hue, through which the viscera and accompanying structures are seen to project into the dilated root of the umbilical cord.

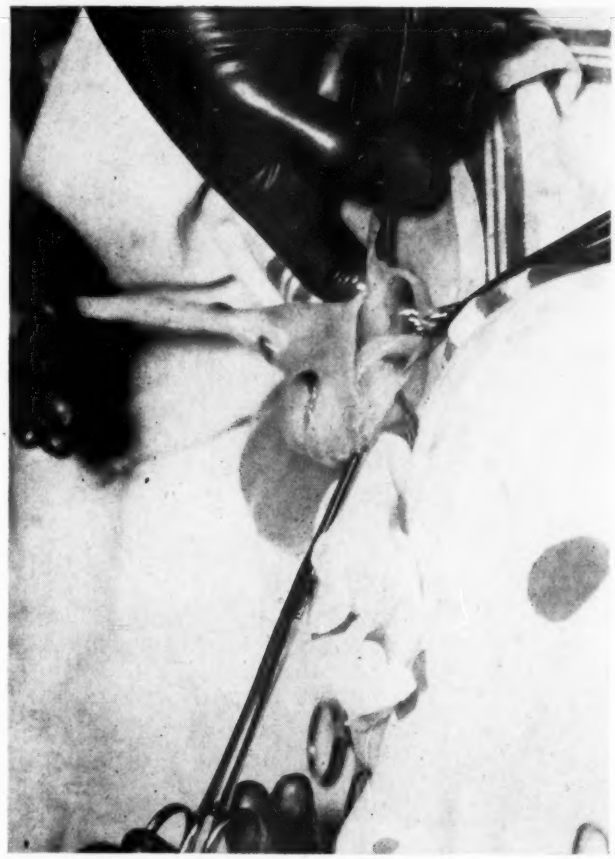


Fig. 4.—Closure of sac after reduction of contents (local anesthesia).

Although translucent and moist at birth, dehydration soon ensues and the sac becomes dry and friable, frequently tearing on manipulation. Should evisceration then occur, shock and death will be the inevitable result.

Eventration of less degree takes a variable form. The defect may consist in the mere thickening of the umbilical cord or in an obvious protrusion of intestinal content.

DIAGNOSIS

There is a protrusive mass in the umbilical cord, with a grayish, translucent veil, beneath which the adumbrated viscera are enclosed.

TREATMENT

In complete exomphalos treatment is obviously of no avail.

A small herniation into the umbilical cord is frequently curable in the newborn infant by means of a retaining apparatus, that is, adhesive plaster strapping containing an enclosed small button or a coin.

Fig. 5.—Ten days after operation.

SURGICAL

The surgical treatment of this emergency is customarily carried out, when not contraindicated, soon after birth—within the first twelve hours. It has been widely observed that a newborn infant usually bears surgical procedures remarkably well if they are not too extensive or prolonged.

Local anesthesia only should be used.

TABLE I

CONTENTS OF OMPHALOCELE

CASE	AGE (HR.)	SEX	DIAMETER OF OMPHALOCELE (CM.)	INTESTINE	COLON	LIVER	OTHER VISCERA	TREATMENT	RESULT
1	1	F	10	Plus	Plus	0	0	Surgery	Died
2	2	F	10	Plus	0	0	0	Surgery	Cured
3	4	M	7	Plus	Plus	0	0	Surgery	Cured
4	½	F	7	Plus	Plus	0	0	Surgery	Cured

The skin margin should be dissected from the subjacent rectus sheath and transversalis fascia, being careful not to tear or cut the sac wall, for there is danger of injuring a protruding viscus or permitting extrusion of the sac contents. The viscera are placed within the abdominal cavity before opening the sac to eliminate unnecessary trauma, to prevent evisceration and shock, and to obviate the possibility of infection. (See Fig. 4.)

After reduction, the two umbilical arteries and the umbilical vein are ligated.

One or two fingers are inserted into the opening by pressure from without the sac wall to maintain the viscera within the abdominal cavity. A continuous chromic suture, No. 1 or No. 2, on a Mayo needle is then inserted circumferentially to include the posterior rectus sheath and the transversalis fascia. This is then tied carefully so as not to impinge upon a loop of bowel or omentum. The anterior rectus sheaths are then approximated after excising the redundant part of the sac. In this manner it is not necessary to pass a suture through the neck of the sack which tears very easily.

If there is any doubt of the feasibility of approximating the rectus sheaths with a chromic suture, black silk may be used as a through-and-through stitch, including the skin and the abdominal aponeurosis. (See Fig. 5.)

COMPLICATIONS

Respiratory embarrassment may ensue because of displacement of the diaphragm as a result of increased intra-abdominal tension. Cases of paralytic ileus have been reported from pressure on the intestine.

A SHARP DISSECTOR FOR MENISCECTOMY

CAPTAIN RAYMOND E. BUIRGE, MEDICAL CORPS, U. S. ARMY

THE removal of a semilunar cartilage is a common procedure, yet it may still be a rather difficult one in spite of the exposure provided by any incision[1] of choice. An additional posterior capsular incision[2, 3] is often useful in freeing the posterior attachment of the meniscus. Numerous instruments[4-12] have been designed to lessen the difficulties attending the operation of meniscectomy.

The use of an adequate single incision into the joint to accomplish the entire removal of the semilunar cartilage may be desired. Two instruments (Fig. 1) were devised to be used in excision of the medial semilunar cartilage through an anterior incision into the joint.

A modified Jones incision is used in the skin. The incision into the joint extends from a point, the leg hanging at a right angle, 0.5 cm. medial to the apical attachment of the ligamentum patellae obliquely downward and posterior, dividing the fibrous fanlike membrane of the tibial collateral ligament[13] and ending at the parallel fibers on a level with the coronary ligament.

The cartilage is usually freed anteriorly with ease. The liberation of the central portion of the cartilage is begun by the delineation of the superior and inferior capsular reflections which are separately divided along the periphery of the cartilage by the broad sharp dissector. By means of traction tension on the cartilage, the areolar tissue binding the cartilage to the parallel portion of the tibial collateral ligament is made taut and easily separated with the dissector.

The oblique portion of the tibial collateral ligament is inseparably united to the joint capsule posteriorly and, accordingly, has been demonstrated[14] to be joined to the meniscus. The knee is hyperflexed which allows the tibial collateral ligament to slide backward,[13] permitting easier access to the posterior capsular attachment of the cartilage. The limited exposure can be further improved by adduction or abduction and rotation of the tibia on the femur combined with digital pressure on the posterior joint capsule. The narrow dissector is employed to divide the superior and inferior capsular folds and the fibrous tissue uniting the capsule and the fibrocartilage. The freed cartilage is dislocated into the intercondylar notch, and its posterior limb between the lateral meniscus and the posterior cruciate ligament is divided under direct vision with the broad dissector.

Received for publication, May 6, 1944.

These instruments were found to be a satisfactory addition to the usual devices used to remove the semilunar cartilage.[15] They are readily constructed* from sharp periosteal elevators.

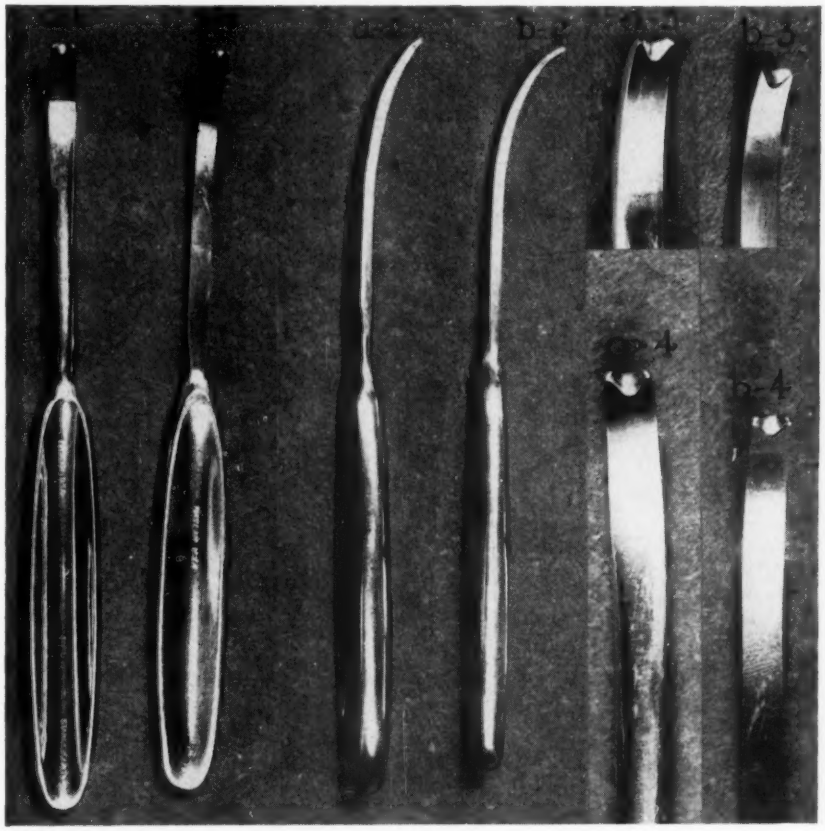


Fig. 1.—Photograph of cartilage dissectors. *a-1*, 4/5 actual size; broad dissector. *b-1*, 4/5 actual size; narrow dissector. *a-2*, side view, curved approximately 115 degrees. *b-2*, curved approximately 130 degrees. *a-3*, enlarged 1 2/5 times. *b-3*, oblique view of concave cutting edge showing blunted outer margins. *a-4* and *b-4*, end view enlarged 1 2/5 times.

REFERENCES

1. Jones, R., and Lovett, R. W.: Orthopedic Surgery, New York, 1923, William Wood & Co., p. 34.
2. Cave, E. F.: Combined Anterior-Posterior Approach to the Knee Joint, J. Bone & Joint Surg. **17**: 427-430, 1935.
3. Bosworth, David M.: An Operation for Meniscectomy of the Knee, J. Bone & Joint Surg. **19**: 1113-1116, 1937.
4. Steinmann, F.: Fracture Surgery, Internat. Clin. **4**: 221-225, 1926.
5. Fairbank, H. A. T.: Meniscotomy Knife, Lancet **1**: 24, 1929.
6. Leggiadro, Vincent: A New Electric Meniscotomy Knife, J. Bone & Joint Surg. **19**: 246, 1937.
7. Lowe, Frank A., and Breck, Louis W.: A New Knife for Use in Removing Semilunar Cartilages, J. Bone & Joint Surg. **20**: 220, 1938.
8. Haggart, G. E., and Toumey, James W.: Knee Joint Arthrotomy for Removal of a Semilunar Cartilage: Technic of the Lateral and Anterior Incisions, S. Clin. North America **19**: 709-714, 1939.

*Made by Pfc. William Nelson, Medical Detachment, Oliver General Hospital, Augusta, Ga.

9. Mercer, Walter: A New Knife for the Removal of the Meniscus, J. Bone & Joint Surg. **21**: 744, 1939.
10. Dunlap, K.: Method for Complete Removal of the Semilunar Cartilage, J. Bone & Joint Surg. **24**: 929-931, 1942.
11. Mitchell, Alexander: Meniscotomy Knife, Lancet **244**: 528, 1943.
12. Freiberg, Albert H.: The Removal of the Meniscus From the Knee-Joint, J. Orth. Surg. **3**: 697-698, 1921.
13. Brantigan, O. C., and Voshell, A. F.: The Tibial Collateral Ligament: Its Functions, Its Bursae, and Its Relation to the Medial Meniscus, J. Bone & Joint Surg. **25**: 121-131, 1943.
14. Brantigan, O. C., and Voshell, A. F.: The Mechanics of the Ligaments and Menisci of the Knee Joint, J. Bone & Joint Surg. **23**: 44-66, 1941.
15. Buirge, Raymond E.: Disabilities of the Knee (A Survey of 283 Admissions to the Oliver General Hospital). Unpublished data.

Notices

UROLOGY AWARD

The American Urological Association offers an annual award "not to exceed $500" for an essay (or essays) on the result of some specific clinical or laboratory research in urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deems none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the Secretary, for full particulars.

The selected essay (or essays) will appear on the program of the forthcoming June meeting of the American Urological Association.

Essays must be in the hands of the secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tenn., on or before March 15, 1945.

AMERICAN COLLEGE OF SURGEONS EXPANDS GRADUATE TRAINING PROGRAM

In expanding its program of Graduate Training in Surgery to assure adequate opportunities for advanced training in surgery, particularly for recent medical graduates when they return from service with the Armed Forces, the American College of Surgeons has enlarged its headquarters staff in Chicago and announces the following new appointments effective immediately:

Major General Charles R. Reynolds (M.C., Retired), former Surgeon General of the U. S. Army, has been appointed Consultant in Graduate Training in Surgery. General Reynolds was in the Army from 1900 to 1939; served in the Philippine Insurrection; was Chief Surgeon of the Second Army, A.E.F., in World War I; was Commandant of the Army Field Service Medical School, Carlisle, Pa., from 1923 to 1931; and was Surgeon General of the Army from 1935 to 1939. He has been Director of the Tuberculosis Control Program of the Pennsylvania State Health Department for the past four years.

Dr. George H. Miller, formerly Dean of the Faculty of Medicine and Chairman and Professor of the Department, American University of Beirut, Lebanon, Syria, has been appointed Director of Educational Activities. Dr. Miller served in the U. S. Army Medical Corps, A.E.F., in 1918 and 1919; was Associate Professor of Pharmacology and later Associate Professor of Medicine of the State University of Iowa College of Medicine between 1922 and 1932; and was with the American University of Beirut from 1932 to 1944.

The Department of Graduate Training in Surgery is under the general direction of Dr. Malcolm T. MacEachern, Chairman of the Administrative Board, working with that board, and responsible to the Committee on Graduate Training in Surgery, of which Dr. Dallas B. Phemister of Chicago is chairman, and to the Board of Regents. In addition to General Reynolds and Dr. Miller, the staff of the department consists of Dr. Paul S. Ferguson, Director of Surveys, and three assistants who conduct the surveys, and the field representatives conducting the regular Hospital Standardization surverys under the direction of Dr. E. W. Williamson, Assistant Director of the College, who assist as required in the graduate training program. The latter is a development of the basic work of the college in stimulating the improvement of hospital service.

Surveys of hospitals for Graduate training in Surgery have been conducted since 1937 by the college. When the war ends in Europe, in order to satisfy the demands of men whose training in surgery was interrupted by war service, together with those of current medical graduates, sufficient opportunities should be ready in order to offer approved training to men who wish to become surgeons, Dr. MacEachern declares, adding that a competent surgeon according to present-day ideas requires a preparation of three or more years of systematic, supervised graduate training in general surgery or a surgical specialty, following a general internship and graduation from an acceptable medical school.

Book Reviews

Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgement of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

SURGICAL CLINICS OF NORTH AMERICA. Lahey Clinic Number. Cloth. Pp. 740, with 275 illustrations. Philadelphia, 1944, W. B. Saunders Company.

TEXTBOOK OF GYNECOLOGY. By Emil Novak, M.D., F.A.C.S. Cloth. Price $8. Pp. 708, with 456 illustrations. Baltimore, 1944, Williams & Wilkins Company.

SURGICAL DISORDERS OF THE CHEST. By J. K. Donaldson, Major Medical Corps. Cloth. Price $6.50. Pp. 364, with 127 illustrations. Philadelphia, 1944, Lea & Febiger.

HYPERTENSION AND HYPERTENSIVE DISEASE. By Goldring and Chasis, New York University College of Medicine. Cloth. Price $3.50. Pp. 253. New York, 1944, Commonwealth Fund.

X-RAY EXAMINATION OF THE STOMACH. By Fredric E. Templeton, Department of Roentgenology, The Cleveland Clinic. Cloth. Price $10. Pp. 516. Chicago, 1944, University of Chicago Press.

THE ART OF ANESTHESIA. By Dr. Paluel J. Flagg, Visiting Anesthetist to Manhattan Eye and Ear Hospital. Cloth. Price $6. Pp. 506. Philadelphia, 1944, J. B. Lippincott Company.

A HANDBOOK OF ROENTGEN DIAGNOSIS OF THE GASTROINTESTINAL TRACT. By Fred Jenner Hodges, B.S., M.D., Professor of Roentgenology, University of Michigan Medical School, Ann Arbor, Mich. Cloth. Price $5.50. Pp. 320. Chicago, 1944, The Year Book Publishers, Inc.

EMERGENCY SURGERY. By Hamilton Bailey, F.R.C.S., Surgeon, Royal Northern Hospital, London. Cloth. Price $18. Pp. 969, with 1039 illustrations. Baltimore, 1944, Williams & Wilkins Company.

CATARACT AND ANOMALIES OF THE LENS. By John G. Bellows, M.D., Ph.D., Assistant Professor of Ophthalmology, Northwestern University Medical School, Chicago. Cloth. Pp. 624, with 208 illustrations and 4 color plates, St. Louis, 1944, The C. V. Mosby Co.

CLINICAL UROLOGY, Vol. 1 and Vol. 2. By Oswald Swinney Lowsley, Director Department of Urology of the New York Hospital and Thomas Joseph Kirwin, Attending Surgeon of the Department of Urology of the New York Hospital. Cloth. Price $10 per set. Pp. 942 (Vol. 1) and pp. 1769 (Vol. 2). Baltimore, 1944, Williams & Wilkins Company.

METABOLISM MANUAL. By Jessie Lex, ASCP, R.T., M.T., President Illinois Society Clinical Laboratory Technicians, Peoria, Ill. Cloth. Pp. 56. Baltimore, 1943, The Waverly Press.

THE FLOW OF WATER THROUGH THE KIDNEY. By Dr. Felix Fuchs. Cloth. Pp. 100. New York, 1944, Commonwealth Fund.

GYNECOLOGY AND GYNECOLOGIC NURSING. By Norman F. Miller, M.D., Professor of Obstetrics and Gynecology, University of Michigan Medical School. Cloth. Price $2.75. Pp. 378, with 227 illustrations. Philadelphia, 1944, W. B. Saunders Company.

OPERATIONS OF GENERAL SURGERY. By Thomas G. Orr, M.D., Professor of Surgery, University of Kansas, School of Medicine, Kansas City, Kan. Cloth. Pp. 723, with 1396 illustrations and 570 figures. Philadelphia, 1944, W. B. Saunders Company.

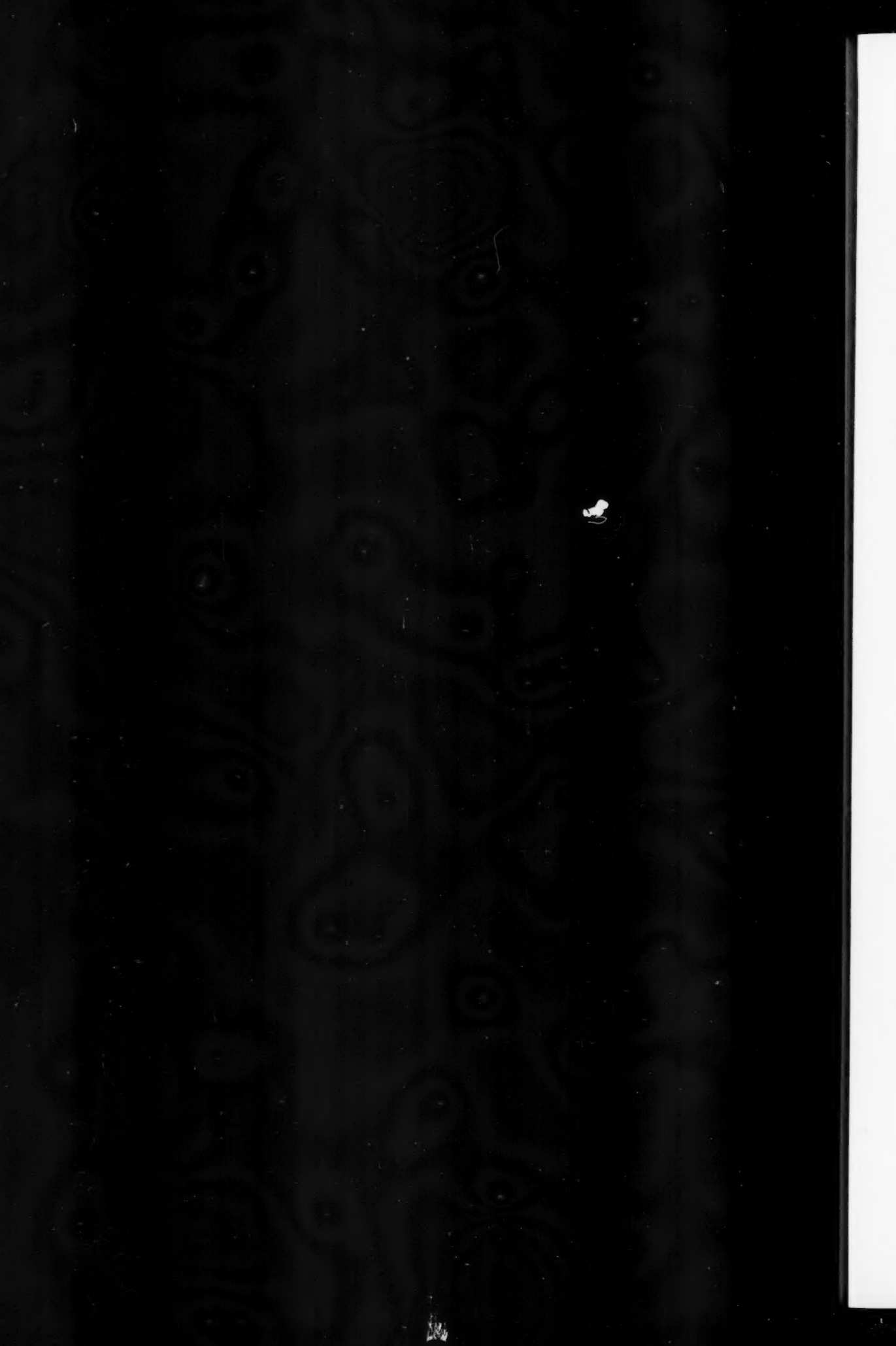
STRUCTURE AND FUNCTION AS SEEN IN THE FOOT. By Frederic Wood Jones, D.Sc., Professor of Anatomy, University of Manchester. Cloth. Price $7.50. Pp. 329. Baltimore, 1944, Williams & Wilkins Company.

THE RADIOLOGY OF BONES AND JOINTS. By James F. Brailsford, M.D., Ph.D., Hunterian Professor Royal College of Surgeons, England. Cloth. Price $12. Pp. 440, with 404 illustrations. Baltimore, 1944, Williams & Wilkins Company.

ORTHOPAEDIC SURGERY. By Walter Mercer, M.B., Assistant Surgeon, Royal Infirmary, Edinburgh. Cloth. Price $12. Pp. 947. Baltimore, 1943, Williams & Wilkins Company.

DISEASES OF THE DIGESTIVE SYSTEM. By Sidney A. Portis, Associate Professor of Medicine, University of Illinois Medical School. Cloth. Pp. 932, with 182 illustrations. Philadelphia, 1944, Lea & Febiger.

PRINCIPLES AND PRACTICE OF SURGERY. By W. Wayne Babcock, M.D., Philadelphia General Hospital, Philadelphia. Cloth. Pp. 1331, with 1141 illustrations and 8 colored illustrations. Philadelphia, 1944, Lea & Febiger.



IN WARTIME ANESTHESIA

MILITARY MEN[1] writing on wartime anesthesia state that a heavy solution of Nupercaine* (1:200) affords anesthesia of long duration with no circulatory disturbances in their series. Furthermore, they note that Nupercaine Hydrochloride is highly useful for rectal operations and serves admirably for high abdominal anesthesia.

As a spinal anesthetic, Jones solution (Nupercaine 1.1500) — which is receiving enthusiastic acclaim by the British — may be used in the management of thoracic war injuries[2].

NUPERCAINE

a long-acting anesthetic

[1] Clement, F.; Elder, C.: Anesthesiology, 4:516, 1943.

[2] Forsee, J.; Shefts, L.; Burbank, B.; Fitzpatrick, L.; Burford, T.: J. Lab. & Clin. Med., 28:418, 1943.

ACCEPTED AMERICAN MEDICAL ASSN

*Trade Mark Reg. U. S. Pat. Off. Word "Nupercaine" identifies the product as alpha-butyloxycinchoninic acid - gamma - diethylethylenediamide-hydrochloride.

ARMY (E) NAVY

Tomorrow's Medicines from Today's Research

Ciba

Pharmaceutical Products, Inc.

SUMMIT, NEW JERSEY

CANADIAN BRANCH: MONTREAL, QUEBEC

"I hear the war's practically over... back home!"

PROBABLY it's only natural for us here at home to feel that the war's almost won, the way the good news has been pouring in.

But the war's not over for *him—not by a long sight!* And he's just one of a few million or more that will stay over there until they finish the bloody mess. Or kill time for a few months—or years—in some hospital.

What about *you?*

This is no time to relax. No time to forget the unfinished business. It's *still* your war, and it *still* costs a lot.

So dig down deep this time. Dig down till it hurts, and get yourself a hundred-dollar War Bond over and above any you now own—or are now purchasing. This 6th War Loan is every bit as important to our complete and final Victory as was the first.

Don't "let George do it"—get *yourself* that *added* bond, help finish a magnificent job *right.* The quicker you reach down deep, the better you do *your* job for war, the more you'll contribute to ending the fight. And the quicker they'll come back—the guys that can *still* be killed.

After all, you're safe and sound and *home. That's worth another hundred-dollar bond to you, isn't it?*

6th WAR LOAN

Buy at least one extra $100 War Bond today!

The C. V. Mosby Company — Publishers — St. Louis 3, Mo.

★ *This is an official U. S. Treasury advertisement—prepared under auspices of Treasury Department and War Advertising Council.* ★

LIPPINCOTT SELECTED PROFESSIONAL BOOKS

"Will I ever use these again?"

What assurance can you give this despairing patient? Today, hand injuries lead the list of industrial accidents. War, too, is crippling strong, young hands in appalling numbers.

America's doctors—general practitioner and specialist, alike—must be ready to meet this real challenge with precise, up-to-the-minute knowledge and skill.

Dr. Sterling Bunnell's outstanding, new book, *Surgery of the Hand*, gives every doctor confronted by hand injuries the last word in the specialized field of reconstructive hand surgery.

Dr. Bunnell's knowledge is helping America's doctors to say with assurance, "*You will use your hands again!*"

SURGERY OF THE HAND

STERLING BUNNELL, M.D.

STERLING BUNNELL, M.D., is one of the men in all the world best qualified to write on the diagnosis and treatment of hand injuries. He is internationally known and recognized. His professional societies include: Honorary Member of the American Academy of Orthopedic Surgeons; Member of the American Association of Surgery of Trauma, American Society of Plastic and Reconstructive Surgery, Licentiate of the American Board of General Surgery and American Board of Plastic Surgery.

WHAT MUST THE HAND SURGEON KNOW?

Surgical reconstruction of the hand involves a composite knowledge of orthopedic, plastic and neurologic surgery. Highest success requires competency in all three fields. *Surgery of the Hand* has been written specifically to give a thorough working knowledge of these three specialties.

DESTINED FOR GREATNESS

750 PAGES • 600 ILLUSTRATIONS • $12.00

DESERVED ACCLAIM!

The unprecedented volume of orders received just before publication consumed an unusually large first printing. A new second printing went to press immediately after publication release. If your copy is delayed a few days in delivery, we feel you will understand.

PUBLISHED OCTOBER 3, 1944 — 2nd Printing OCTOBER, 1944

A LIPPINCOTT SELECTED PROFESSIONAL BOOK — DROIT ET AVANT

J. B. LIPPINCOTT COMPANY, Philadelphia 5, Pa. S-12-44

Enter my order and send me Bunnell's *Surgery of the Hand*, $12.00 ☐ Charge my account ☐ Cash enclosed

SEND TO: NAME_____

STREET ADDRESS_____

CITY AND STATE_____

Under your guarantee, I may return the book in 10 days, otherwise I will pay in full within 30 days.

LIPPINCOTT SELECTED PROFESSIONAL BOOKS

SURGERY

Editors: ALTON OCHSNER, M.D., 1430 Tulane Ave., New Orleans, La., and OWEN H. WANGENSTEEN, M.D., University Hospitals, Minneapolis, Minn.

Associate Editor: ALFRED BLALOCK, M.D., Johns Hopkins Hospital, Baltimore, Md.

Published by THE C. V. MOSBY COMPANY, 3525 Pine Blvd., St. Louis (3), U.S.A.

Great Britain Agents: Henry Kimpton, Ltd., 26 Bloomsbury Way, London, W.C.1.
Entered at the Post Office at St. Louis, Mo., as Second-Class Matter.

Published Monthly. Subscriptions may begin at any time.

Editorial Communications

Original Communications.—This Journal invites concise original articles of new matter in the broad field of clinical and experimental surgery. Descriptions of new techniques and methods are welcomed. Articles are accepted for publication with the understanding that they are contributed solely to SURGERY.

Manuscripts submitted for publication may be sent to Dr. Alton Ochsner, 1430 Tulane Avenue, New Orleans, Louisiana, or to Dr. Owen H. Wangensteen, University Hospitals, Minneapolis, Minnesota.

Neither the editors nor the publishers accept responsibility for the views and statements of authors expressed in their communications.

Translations.—Manuscripts written in a foreign language, if found suitable for publication, will be translated without cost to the author.

Manuscripts.—Manuscripts should be typewritten on one side of the paper only, with double spacing and liberal margins. References should be placed at the end of the article and should conform to the style of the Quarterly Cumulative Index Medicus; viz., name of author, title of article, and name of periodical with volume, page, and year. Illustrations accompanying manuscripts should be numbered, provided with suitable legends, and marked on margin or back with the author's name.

Authors should indicate on the manuscript the approximate position of text figures. The original drawings, not photographs of them, should accompany the manuscript.

Illustrations.—A reasonable number of half-tone illustrations will be reproduced free of cost to the author, but special arrangements must be made with the editors for color plates, elaborate tables or extra illustrations. Copy for zinc cuts (such as pen drawings and charts) should be drawn and lettered only in India ink, or black typewriter ribbon (when the typewriter is used), as ordinary blue ink or colors will not reproduce. Only good photographic prints or drawings should be supplied for half-tone work.

Exchanges.—Contributions, letters, exchanges, reprints, and all other communications relating to SURGERY should be sent to one of the editors.

Review of Books.—Books and monographs, native and foreign, will be reviewed according to their merits and as space permits. Books may be sent to Dr. Owen H. Wangensteen, University Hospitals, Minneapolis, Minn.

Reprints.—Reprints of articles published among "Original Communications" must be ordered directly through the publishers, The C. V. Mosby Co., 3523 Pine Blvd., St. Louis (3), U. S. A., who will send their schedule of prices.

Business Communications

Business Communications.—All communications in regard to advertising, subscriptions, change of address, etc., should be addressed to the publishers, The C. V. Mosby Company, 3523 Pine Blvd., St. Louis (3), Mo.

Subscription Rates.—Single copies, 85 cents. To any place in the United States and its Possessions and the Pan-American Countries, $10.00 per year in advance. To Canada, $11.50 (Canadian Currency), and under foreign postage, $11.00. Includes two volumes a year, January and July.

Remittances.—Remittances for subscriptions should be made by check, draft, post office or express money order, or registered letter, payable to the publishers, The C. V. Mosby Co.

Change of Address.—The publishers should be advised of change of subscriber's address about fifteen days before the date of issue, with both new and old addresses given.

Nonreceipt of Copies.—Complaints for nonreceipt of copies or requests for extra numbers must be received on or before the 10th of the month preceding publication; otherwise the supply is likely to be exhausted.

Advertisements.—Only articles of known scientific value will be given space. Forms close tenth of month preceding date of issue. Advertising rates and page sizes on application.

NEW SURGICAL WORKS

NEW WORK *JUST READY*

PRINCIPLES AND PRACTICE OF SURGERY

BY W. WAYNE BABCOCK, M.D., F.A.C.S.

Emeritus Professor of Surgery, Temple University; Acting Consultant, Philadelphia General Hospital.

With the Collaboration of Thirty-Seven Members of the Faculty of Temple University

Imperial octavo, 1331 pages, illustrated with 1141 engravings and 8 colored plates. Cloth, $12.00

This important new work avoids both the weakness of single authorship and the omissions, duplications and conflicting statements of multiple authors who live in separate parts of the country and supply individual chapters. Most of the thirty-seven collaborators in this text work together in the hospital and medical school of Temple University. Their material has been collected, condensed and largely rewritten. The result has made possible the incorporation of much detail of modern surgical practice never before included in a single volume. Conflicting opinions have been reconciled by discussion and duplications largely deleted by the use of cross references.

Besides the rarer surgical conditions often omitted or merely mentioned in surgical texts, the common surgical conditions, operations, techniques, the special instruments, drugs, chemicals, sutures, drains and dressings used by the surgeon are all described in relation to their best application. The work covers practically every method of surgical diagnosis and treatment. Each of the contributors is either a teacher or specialist in the field which has been assigned to him. The work presents an enormous amount of information excellently organized and absolutely authoritative. The numerous illustrations are mostly original and the work is a safe guide in every problem.

NEW WORK *JUST READY*

SURGICAL DISORDERS OF THE CHEST

Diagnosis and Treatment

By J. K. DONALDSON, M.D., F.A.C.S.

Major, M.C., Army of the United States; Diplomate American Board of Surgery; Associate Professor of Surgery in Charge of Thoracic Surgery, University of Arkansas School of Medicine, etc.

Octavo, 364 pages, illustrated with 127 engravings. Cloth, $6.50

This new work enables physicians and surgeons who have been unable to follow the rapid advances that have been made in the thoracic field through the last decade to develop the new concepts of chest disorders in the light of vastly improved therapeutic possibilities. It is on the general practitioner that the patient depends for diagnosis and advice and he is the first to see the majority of these cases. Early diagnosis and proper recommendations are of the first importance.

The full discussion pertaining specifically to war injuries has been included. This work should so increase the diagnostic efficiency of the general practitioner that the patient will be brought to the chest surgeon's attention at the earliest possible moment. It will assist him to evaluate the practicability of major procedures. Even in those cases which only the chest surgeon should attempt to execute, the general surgeon and general practitioner should be part of a well-coordinated team.

LEA & FEBIGER

WASHINGTON SQUARE
PHILADELPHIA 6, PA.

Please send me book(s) checked: ☐ Check enclosed herewith ☐ Bill me at 30 days

☐ Babcock's Principles and Practice of Surgery ---------- $12.00

☐ Donaldson's Surgical Disorders of the Chest ---------- 6.50

Name---------- Address----------

S. 12-44

M E M O R A N D U M

Fight INFANTILE PARALYSIS
1945 JANUARY 1945
S M T W T F S
14 15 16 17 18 19 20
21 22 23 24 25 26 27
28 29 30 31
JOIN THE MARCH OF DIMES

To: Mr. & Mrs. America
From: Your Children
Re: THE MARCH OF DIMES

DON'T FORGET--that last summer America experienced one of its worst epidemics of infantile paralysis.

DON'T FORGET--that infantile paralysis invades the homes of rich and poor, weak and strong alike, and is no respector of age, race, creed or color.

DON'T FORGET--your dimes and dollars made possible the vital aid rendered by The National Foundation for Infantile Paralysis during the epidemic crisis.

DON'T FORGET--how infantile paralysis might have sabotaged our tremendous war production effort if it had not been countered by your dimes and dollars.

JAN. 14-31

DON'T FORGET--that no one can predict where polio will strike in 1945! Prepare to keep America's children STRONG!

Send your dimes and dollars to
President Roosevelt
at
The White House.

Authoritative — Up-to-the-Minute — Complete

CURRENT OBSTETRICS AND GYNECOLOGY

Proceedings of the Second

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

A correlated program of essays, panel discussions and symposia epitomizing everything important and new in the fields of obstetrics and gynecology. The subject material, carefully integrated in advance, is presented under the strict criteria of question and answer discussions. Authors are unimpeachable authorities—each in his respective field. Discussors are especially selected for experience, critical ability. Analyses and summaries are—as a result—the last word. No stone is left unturned. The result is:

A Work Absolutely Essential to Specialist, General Practitioner, Nurse, Hospital Executive and Maternal and Child-Welfare Worker

Among the Contributors Are:

Fred L. Adair	Nicholson J. Eastman	Edward Allen
Aura E. Severinghaus	Herbert E. Schmitz	Robert D. Mussey
Robert Latou Dickinson	E. D. Plass	J. P. Greenhill
G. D. Royston	I. C. Rubin	E. G. Waters
Carl G. Hartman	Abner I. Weisman	Harry W. Mayes
R. S. Siddall	David S. Hillis	Alan F. Guttmacher
John L. Parks	Lewis C. Scheffey	Philip Levine
Alex E. Brown	A. W. Diddle	A. N. Arneson
E. Granville Crabtree	James R. Reinberger	Sidney O. Levinson
Curtis J. Lund	Lyman W. Mason	Paul F. Fletcher

and over sixty others

I *Almost every important teaching institution represented.*

II *Obstetrics, Gynecology, Obstetrical Hospital Management, Obstetrical Nursing, Public Health and Social Service Aspects.*

III *A complete correlated refresher course absolutely up to date.*

Price, $5.50

PUBLISHED BY THE WESTERN JOURNAL OF SURGERY PUBLISHING COMPANY, PORTLAND, OREGON, FOR THE AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

To: 12-44

THE AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY
650 Rush Street
Chicago, Illinois

Please place my order for one copy of the 1942 Transactions, at $5.50 per volume, for which check is enclosed (or) you may bill me when volume is shipped.

Name _____ M.D.

Address _____ City _____ State _____

INDEX TO ADVERTISERS

Please mention "SURGERY" when writing to our advertisers—It identifies you

American Congress on Obstetrics and Gynecology, The ---- 19
Articles to Appear in Early Issues---- 3rd Cover
Bard-Parker Company, Inc. Rib-Back Blades) ---- 1
Ciba Pharmaceutical Products, Inc. (Nupercaine) ---- 13
Davies & Geck, Inc. (Kalmerid Germicidal Tablets) ---- 3
Emerson Hotel, The (Baltimore, Md.) ---- 20
Ethicon Suture Laboratories (Catgut Sutures) ---- Insert between pp. 10 and 11
Gilmer Binder, The (Journal Binder) ---- 20
Hoffmann-La Roche, Inc. (Pantopon) ---- 4th Cover
Iodine Educational Bureau, Inc. (Iodine) ---- 8
Lea & Febiger (Surgical Books)---- 17
Lilly and Company, Eli ---- 12
Lippincott Company, J. B. (Surgical Books) ---- 15
March of Dimes ---- 18
Merrell Company, The Wm. S. (Sulfa-Ceepryn Cream) ---- 9
O'Leary, Inc., Lydia (Covermark)-- 10
Owens-Corning Fiberglas Corporation (Fiberglas) ---- 7
Singer Sewing Machine Company (Surgical Stitching Instrument)-- 4
Sklar Manufacturing Company, J. (Stainless Steel Instruments) ---- 11
Squibb & Sons, E. R. (Aluminum Hydroxide Gel) ---- 6
Squibb & Sons, E. R. (Basic Formula Vitamin Tablets) ---- 2
Stearns & Company, Frederick (Parenamine Amino Acids) ---- 5
War Bonds ---- 14

All possible care is exercised in the preparation of this index. The publishers are not responsible for any errors or omissions.

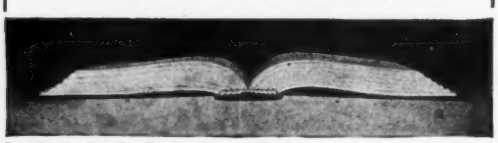
Make a Real REFERENCE BOOK OF YOUR JOURNAL

File each copy as soon as received so it will be instantly available when you want to refer to a recent article. We have secured what we believe to be the best binder made for this purpose. It is light, easy to operate, and handsome, and opens perfectly flat for easy reference.

Binder to hold 1 volume (6 issues) PRICE, $2.00

Binder to hold 2 volumes (12 issues—1 year) PRICE, $2.50

(Specify one you wish sent)



PRODUCED BY GILMER

Individual name or date and volume number will be stamped in gold on back of each binder for 50c. Sent postpaid on receipt of check or money order, with a guarantee that if you are not more than satisfied, your money will be refunded.

Be sure to state that the binder is intended for use with this Journal.

Address The Gilmer Binder
307 New Street, Philadelphia, Pa.

FOR THE EXACTING GUEST

It's Baltimore's Best

—best for accommodations that provide a monopoly on luxury.
—best for location that places you in the principal downtown district, near business contacts and pleasure places.
—best for streamline service that offers you all the modern guest facilities.
—best because of these moderately priced public rooms—

MAIN DINING ROOM, NEW CHESAPEAKE LOUNGE, COFFEE SHOP

450 Large Guest Rooms

All rooms with bath, radio, and circulating ice water.

Single Rooms With Bath, $3.00 up
Double Rooms With Bath, $4.50 up

The Emerson HOTEL
BALTIMORE, MD. O.G. CLEMENTS, MGR.

DEC -6 19-5

Articles to appear in early issues of

SURGERY

CONGENITAL ABSENCE OF THE GALL BLADDER.
By Claude F. Dixon, M.S., M.D., and A. L. Lichtman, M.D., Rochester, Minn.

COTTON SUTURES IN SURGERY OF WARFARE.
By Lieutenant Colonel Robert S. Sparkman, Medical Corps, Army of the United States.

TRAUMATIC PERFORATION OF THE COLON AS SEEN IN A GENERAL HOSPITAL.
By Major Bentley P. Colcock, Medical Corps, U. S. Army.

A NEW HEMOSTATIC CLAMP.
By Cubero O. Gonzalo, M.D., San José, Costa Rica.

THE PREVENTION OF STAPHYLOCOCCUS INFECTIONS OF THE PERITONEUM.
By Rollin A. Daniel, Jr., M.D., and Thomas J. Holbrook, M.D., Nashville, Tenn.

APPENDICITIS AND THE SULFONAMIDE DRUGS.
By Robert L. Sewell, M.D., Fort Worth, Texas.

THE SURGICAL AND ANATOMIC SIGNIFICANCE OF THE MAMMILLARY TUBERCLE OF THE LAST THORACIC VERTEBRA.
By Emanuel B. Kaplan, M.D., F.A.C.S., New York, N. Y.

EXTENSIVE VARICOSITIES OF THE LEG ORIGINATING FROM THE GLUTEAL VEIN.
By William H. Prioleau, M.D., F.A.C.S., Charleston, S.C.

MODIFIED CALIBRATED SKIN GRAFTING KNIFE: FURTHER OBSERVATIONS.
By Major Kerwin M. Marcks, Medical Corps, U. S. Army.

ANESTHESIA FOR THE BURNED PATIENT.
By Captain E. M. Papper, Medical Corps, Army of the United States.

TREATMENT OF TENDONS IN FINGER AMPUTATIONS AND DESCRIPTION OF A NEW INSTRUMENT.
By Lieutenant Commander George V. Webster, Medical Corps, U.S.N.R.

ORTHOPEDIC SURGERY FOR RECONSTRUCTION OF CONGENITAL MALFORMATIONS OF THE KIDNEY.
By Robert Gutierrez, A.B., M.D., F.A.C.S., New York, N. Y.

THE SENSATION OF GAS STOPPAGE DURING THE ONSET OF ACUTE APPENDICITIS.
By E. L. Keyes, St. Louis, Mo.

TRAUMATIC OSTEOCHONDRITIS OF THE PATELLA.
By Major Francis J. Cox, Medical Corps, U. S. Army.

THE ALLERGIC PATHOGENETIC MECHANISM OF THYROTOXICOSIS.
By Abraham O. Wilensky, M.D., New York, N. Y.

CERTAIN SULFONAMIDES AND CERTAIN DERIVATIVES OF ASCORBIC ACID IN EXPERIMENTAL GAS GANGRENE IN WOUNDED MICE.
By Francis J. Ryan, Ph.D., Robert Ballentine, Ph.D., Lillian K. Schneider, A.B., and Gwendolynn M. Tuck, A.B., New York, N. Y.

THE INFLUENCE OF THE LOCAL APPLICATION OF SULFATHIAZOLE ON THE INCIDENCE OF INFECTIONS IN SURGICAL INCISIONS.
By Robert H. More, M.D., Toronto, Canada.

A FOREIGN BODY WITHIN THE PERICARDIUM SUCCESSFULLY REMOVED.
By Major Thomas Duval Watts, and Major Elam C. Toone, Medical Corps, U. S. Army.

CRANIOPLASTY WITH TANTALUM PLATE.
By Dean H. Echols, M.D., and J. A. Colclough, M.D., New Orleans, La.

INTRAPERITONEAL ABSORPTION PATTERNS OF SULFONAMIDES WITH SPECIAL REFERENCE TO MICROCRYSTALLINE SULFATHIAZOLE AND A COMPARISON OF COINCIDENT CONCENTRATIONS IN THE PORTAL VEIN, SYSTEMIC CIRCULATION, AND PERITONEAL FLUID.
By Major Alexander E. Pearce, Medical Corps, Army of the United States, John G. Reinhold, Ph.D., Rose Polonsky Feldman, B.A., and John O. Bower, M.D., F.A.C.S., Philadelphia, Pa.

THE CONSERVATIVE AND OPERATIVE TREATMENT OF LESIONS OF THE INTERVERTEBRAL DISCS IN THE LOW BACK.
By J. Albert Key, M.D., St. Louis, Mo.

Whole opium in a single ampul

Pantopon 'Roche' contains not merely morphine—but *ALL* the other alkaloids of opium. This combination affords a better balanced, smoother opiate action with less likelihood of unpleasant by-effects . .

HOFFMANN-LA ROCHE, INC.

Nutley 10, New Jersey.